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Volume 38

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Symposium on the Lung

Observations on the History of the Bronchopulmonary Segments

EDWARD A. BOYDEN, Ph.D. (Med. Sc.)

Seattle, Washington

IN introducing this series of papers concerning the lung, it is instructive to look back over the seventy-five years in which current knowledge of the segmental anatomy of the lungs has developed, and to see what manner of men were responsible for it.

Prior to the year 1880, little attention had been paid to the mode of branching of the bronchial tree except in its peripheral portions. Generally, the mode was considered to be dichotomous and symmetrical. This concept was changed by a Swiss anatomist, Christoph Theodor Aeby, who presided over the anatomical institute at Bern for twenty-one years.

His interest in the lungs began in 1878, when he injected the trachea of an intact cadaver with Wood's metal. This taught him that the air passage which was most directly continuous with the trachea was the right bronchus and not the left, as had been supposed hitherto. Also, he was struck with the asymmetry of the tracheobronchial tree, noting for the first time that the upper lobe bronchi were differently related to the corresponding pulmonary arteries: the right upper was "eparterial," the left was "hyparterial." Thereupon, he set out to analyze the mode of division of the bronchi in fourteen mammalian families and to homologize the human pattern with that of the lower orders. Especial prominence was given to the interpretation that each lung consisted of an axial stem with alternate dorsal and ventral branches. Thus arose the "doctrine of the stem bronchus" which was to persist on the continent of Europe until the end of the second world war.

Although Aeby moved to Prague toward the end of his career, to succeed Toldt, he belonged to Switzerland. At Basel, he had been a fellow student of the great embryologist-to-be, Wilhelm His, and had absorbed from the less well-known Professor Rütimeyer an undying interest in comparative anatomy. In his fourth year of medicine, he had studied under the great Henle—that genius who had personally redrawn all parts of the human body and created a new gross anatomy—the science we know today. Aeby, too, was endowed with great energy, and with wit and humor. Being a student of Nature, he participated in mountain climbing—an interest just newly developed by civilized man. In the Alps, he climbed at least six of the high peaks—the highest of these in August, 1871—and lived to write an article for Sonntag's *Post* entitled, "A Storm on the Jungfrau." Perhaps it was this stored-up energy which enabled him without the help of even a prosector to teach anatomy, histology and comparative anatomy, to lecture four to six hours a day, and to produce fifty scientific articles and one book before he died from lung disease at the age of fifty.

The second great figure in the history of this subject was William Ewart, pathologist and consulting physician at Brompton and at St. George's Hospital in London. Ewart was obviously the scholarly type of physician, although as a medical student he had voluntarily participated in the Franco-Prussian war—perhaps because of devotion to his mother's country or because he had taken his arts degree at the University of Paris. It is significant that after graduating from Cambridge (M.B. in the first class of the Natural Science Tripos) he became a lecturer in physiology and a demonstrator in physiological

From the Department of Anatomy, University of Washington.

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chemistry, and that after postgraduate work in Berlin, he pressed on to obtain the degree of M.D. at Cambridge. Thus Ewart laid the foundations of knowledge in a field and its literature that was said to be "remarkably intimate and well documented."

However, his was essentially an original mind. His supervision of out-patient practice was said to be "an informative and whimsical demonstration of the various clinical material which came under his eye," and his clinical teaching wholly unlike the stereotyped teaching of the day. Often, patients were disconcerted by his methods of cross examination, and family practitioners felt that he failed to render the prompt and straightforward assistance that was expected of him, because of his preoccupation with the scientific aspects of the disease. "And thus it came about that William Ewart, with great scientific qualities and personal characteristics that endeared him to many, made no headway at all as a consultant physician."

The above sentence—penned after Ewart's death at the age of eighty-one, and concluding the obituary account in *Lancet*—bears the date of 1929. Even then, his "most important literary work" was erroneously considered to be the Gulstonian lectures on "pulmonary cavities." Had he lived only a few years longer, he could have known that his great monograph of 1889—"The bronchi and pulmonary blood vessels: Their anatomy and nomenclature; with a criticism of Professor Aeby's views of the bronchial tree of mammalia and of man"—was to become the cornerstone of an enduring edifice in the history of surgery and medicine.

At the time that Ewart wrote this monograph, the pressing mission of embryology and anatomy was to relate human structure and that of the lower orders into a phylogenetic whole. So Ewart was breasting the current when he took issue with Aeby and asserted that a mammalian pattern should not be read into the structure of human lungs. Many years later, the American anatomist Huntington was to support this view. Meanwhile, Ewart maintained that the shape of the human thorax was such that the bronchi were more radially disposed than in quadrupeds and were not, therefore, dorsal and ventral branches of an axial structure. On this basis, he identified nine major bronchi that supplied respective "districts" of the lungs. If the middle lobe district be divided, these are essentially the bronchopulmonary segments of our day. But the time had not yet come for another step forward. Surgery of the lung and better techniques in anesthesia were virtually unknown; and the comparative anatomists were in the saddle. Hence, Ewart's fruitful ideas had to await a new "millenium"—of four decades; and Aeby's mammalian patterns became the clinical map of the lungs.

In 1934, a brilliant young surgeon of Brompton Hospital, H. P. Nelson, revived Ewart's "districts" and spread the knowledge of them throughout the British Commonwealth. Two years earlier, essentially the same plan had been "discovered" by a young American surgeon. While it has been the intention of the writer not to discuss living contributors at this time, it is necessary at this point to speak of Amiel Glass. Dr. Glass was a surgical interne in Mt. Sinai Hospital in New York when pioneers like Lilienthal were trying to find new ways of treating pulmonary disease. These surgeons impressed upon him the need for locating lesions more precisely. With the aid of the experienced bronchoscopist, Rudolph Kramer, Glass injected the lungs, found eleven "bronchopulmonary segments" and mapped their distribution on the surface of the lungs. While his work in no way compares in breadth and depth with Ewart's, nevertheless it gave new impetus to the study of pulmonary disease in America. Therefore, it is fitting that Glass's work should be an inspiration to young doctors—an example of what may be accomplished when youth concentrates upon specific problems in a chosen field.

For later steps in the development of the concepts of bronchopulmonary segments, the reader is referred to the writer's chapter on the history of this subject.* The purpose of the present article is to call attention to human values in one small field of medicine—to the lives of men who have become dedicated to the advancement of knowledge for its own sake. For much as we may hope that our work will be of use in the world, the driving force to the discovery of new truth is the inquisitiveness of the human mind.

*Segmental Anatomy of the Lungs, Blakiston Division, McGraw-Hill Book Co., 1955.

Pulmonary-Function Tests

WARD S. FOWLER, M.D.

Rochester, Minnesota

THE principal function of the lungs is to provide efficient and adequate exchange of oxygen and carbon dioxide between the atmosphere and the blood. However, this exchange is accomplished not only by the action of the lungs but by the whole complex process of breathing, which involves the medullary respiratory center, the peripheral nerves and muscles, the thoracic wall, the upper airway, the tracheobronchial airway, the pulmonary alveoli and the pulmonary capillary circulation. Emphasis is placed on this fact because disturbances of respiration may arise in any one or several of these sites. Also, the whole respiratory apparatus is involved not only in many so-called pulmonary-function tests but also in the effects of a particular primary abnormality.

In the evaluation of pulmonary function, careful analysis of the history and the results of physical examination is essential. The presence, type, degree and progression of dyspnea merit particular attention. Observation of the patient during and after exercise is often useful. The principal value of pulmonary-function tests is to provide objective measurements. These may be helpful in differential diagnosis and in evaluating pulmonary performance and reserve. Assessment of therapy is often aided by their employment.

Pulmonary-function tests share the limitations of certain other functional tests, such as some used in renal and hepatic disease. A disturbance of the function measured will be detected only if the disease process is sufficiently great. Also, the anatomic or pathologic basis of an abnormality usually must be defined by or in conjunction with other methods of diagnosis. The interpretation of results of pulmonary-function tests, as with most testing procedures, requires their integration with the other aspects of the particular clinical problem.

The most practical tests are those for measuring ventilatory capacity, which is not only affected in various ways by many diseases but is also assessable by tests that can be done easily in a period of minutes with a small recording spirometer of the Benedict-Roth type.* Three procedures are of particular value:

1. The first is the determination of vital capacity, namely, the maximal volume of gas that can be expired following a maximally deep inspiration. Reductions of vital capacity occur with a variety of diseases which affect the ventilatory apparatus, such as poliomyelitis, kyphoscoliosis, and pulmonary alterations associated with fibrosis, emphysema, bronchospasm and vascular congestion.

2. The second procedure is to have the subject perform maximal expiration as *rapidly* as possible. This test gives additional information about the expiratory flow rates that can be achieved with maximal effort. Respiratory obstruction, such as occurs in asthmatic bronchitis and in emphysema, is shown by the prolonged duration and reduced rate of flow of expiration. These abnormalities may be present even though impairment is not sufficiently advanced to produce a definite reduction of the total volume expired (vital

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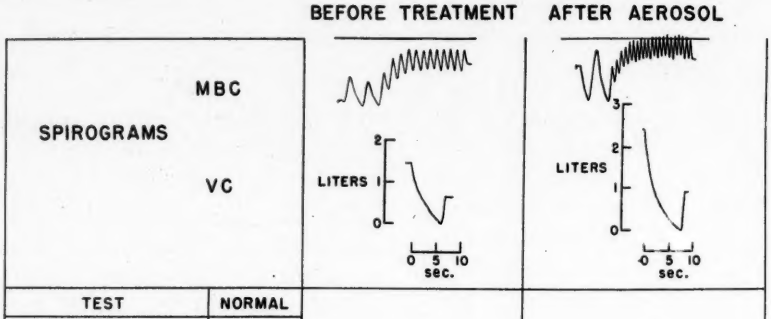
From the Section of Physiology, Mayo Clinic and Mayo Foundation, Rochester, Minnesota. The Mayo Foundation is a part of the Graduate School of the University of Minnesota.

*A conventional cylindrical spirometer of the type used for measurement of basal metabolic rate can be employed, provided the valves and carbon dioxide absorber are removed to reduce resistance to rapid flow of gases. However, spirometers are available commercially (Warren E. Collins, Inc., 555 Huntington Avenue, Boston 15, Massachusetts) with several modifications which make them much more satisfactory for pulmonary-function tests and which can also be used for measurement of metabolic rate. One of the speeds of the recording drum made by this firm is faster than that used for measurement of metabolic rate, and this feature is essential for proper measurement in the tests that involve rapid breathing.

capacity). Figure 1 illustrates the typical expiratory spirograms of a patient with far-advanced asthmatic bronchitis and emphysema. The slow, prolonged expiration is evident both on inspection of the spirograms and on physical examination of the patient. However, in cases of less-advanced emphysema, when physical and roentgenologic examination may give equivocal results, measurement of the forced expiratory spirogram usually reveals definite slowing. The most useful measurements are the percentage of the total volume expired in the first second, which should normally exceed 65 to 70 per cent, and the mean flow rate of the middle half of volume expired (maximal midexpiratory flow), which should normally exceed 2 liters per second. Figure 2 illustrates a different type of spirogram found in other types of pulmonary impairment. The vital capacity is reduced in this case because of pulmonary fibrosis, but air can be expelled with normal rapidity. This has been called "restrictive impairment," in contrast to the obstructive impairment illustrated by the spirograms of the patient with emphysema (Fig. 1).



TEST	NORMAL	BEFORE TREATMENT	AFTER AEROSOL
Vital Capacity (L.)	4.2	1.7	2.4
Max. Breathing Cap. (L./min.)	100	22	38
Max. Midexp. Flow (L./sec.)	>2.0	0.2	0.4
RV/TC (%)	<40	69	54
7 min. N_2 Index (%)	<2.5	10	17
Art. O_2 Saturation (%)	95–98	89	89

Fig. 1. Immediate response to a bronchodilator aerosol in a patient with asthmatic bronchitis and pulmonary emphysema.

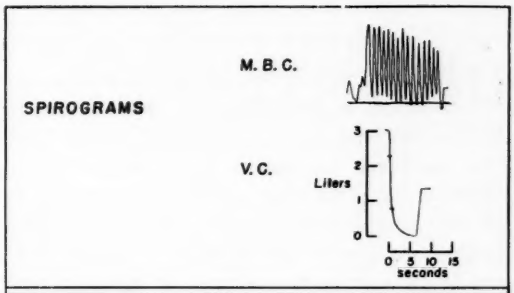
3. The third procedure is the determination of maximal breathing capacity by having the subject breathe as deeply and rapidly as possible for about 15 seconds, as illustrated in Figures 1 and 2, and measuring the volume of gas expired in liters per minute. Maximal breathing capacity is a test of the over-all "bellows" apparatus and may be impaired by skeletal and neuromuscular abnormalities as well as by pulmonary disease. However, only a part of the vital capacity is normally used in this type of rapid and deep breathing, so that relatively large or normal values may be achieved if there is minimal obstruction of the airway, even though the vital capacity is reduced, as for example, in certain types of pulmonary fibrosis and in pulmonary congestion. This is illustrated in Figure 2.

The preceding tests may be used before and after the administration of a bronchodilator drug to assess the extent of readily reversible changes in chronic bronchitis and emphysema, illustrated in Figure 1. It will be noted in this particular case that considerable ventilatory improvement was demonstrated and that this was accompanied by subjective reduction of dyspnea. However, the ventilatory tests still gave grossly abnormal results after treatment, and other measurements, which will be discussed below, failed to show improvement.

Measurement of the residual volume (the volume of gas remaining in the lungs after maximal expiration) must be done by more complex techniques. One standard method is to have the subject breathe 100 per cent oxygen for seven minutes, during which time the nitrogen normally present in the lungs (at a concentration of about 80 per cent) is progressively washed from them into an external bag or spirometer, where its volume may be measured. Normally, a seven-minute period of breathing oxygen will reduce the alveolar concentration of nitrogen to less than 2.5 per cent, but if large portions of the lung are poorly ventilated, their concentration of nitrogen will be reduced less rapidly, so that abnormally high concentrations of nitrogen can be detected by analysis of the alveolar gas delivered by a forced expiration after the seven-minute period. The measurement of residual volume and the detection of retarded alveolar ventilation are facilitated by the use of instruments that have been developed recently for continuous automatic analysis of gases, especially if considerable numbers of patients are to be studied. In emphysema the residual volume is increased both in absolute volume and in its percentage (RV/TC) of the total pulmonary capacity (residual volume plus vital capacity), and the seven-minute nitrogen index is usually elevated (Fig. 1). The case of fibrosis illustrated in Figure 2, in contrast, shows a reduced total capacity and a small nitrogen index.

The preceding tests indicate the performance of both lungs together. However, it may be of assistance to know the relative performance of each lung in situations in which total pulmonary reserve is reduced by bilateral disease and resection is contemplated. One healthy lung can meet the cardiorespiratory requirements, whereas one diseased lung may not. A diseased lung, although appearing aerated on roentgenograms of the thorax, may be contributing either relatively little or much to the over-all exchange of gases, and its removal may produce, respectively, a small or a large impairment. The relative performance of the two lungs can be assessed by bronchospirometry, a method of intubating the trachea and left main bronchus and measuring the vital capacity, ventilation and oxygen consumption of each lung separately.

It is more difficult to evaluate the efficiency with which the lungs maintain the levels of oxygen and carbon dioxide in the arterial blood. Unless arterial hypoxemia is of considerable magnitude, cyanosis (which also depends on other



TEST	NORMAL	——
Vital Capacity (L.)	4.9	3.1
Max. Breathing Capacity (L./minute)	116	100
Max. Midexpiratory Flow (L./second)	> 2.0	2.5
Total Capacity (L.)	6.6	3.9
7 minute N_2 Index (%)	< 2.5	0.3
Arterial O_2 Saturation (%) Rest	95–98	98
Exercise		90

Fig. 2. Results of pulmonary-function tests in a patient with pulmonary fibrosis.

local factors) is detected with difficulty. Ear oximeters, which measure arterial oxygen saturation by the optical characteristics of the blood in the transilluminated pinna of the ear, are useful in the detection of arterial hypoxemia. They can eliminate the necessity for direct chemical analysis of blood obtained by arterial puncture in many cases of suspected hypoxemia, especially if maximal accuracy is achieved by the use of suitable recording apparatus.

Hypoxemia may be produced by one or several of these factors: (1) venous blood passing through poorly ventilated parts of the lung, (2) reduction of pulmonary diffusing capacity, (3) anatomic venous-arterial shunts and (4) depression of total minute volume of alveolar ventilation. The arterial oxygen saturation during or immediately after exercise may be decreased even though normal levels are maintained at rest. This is frequent in certain kinds of pulmonary fibrosis which reduce the diffusing capacity of the lungs without major impairment of the ventilatory capacity, as illustrated in Figure 2. The measurement of arterial oxygen saturation is also useful

(Continued on Page 658)

Clinical Importance of Hypercapnia

E. B. BROWN, JR., and FLETCHER MILLER
Minneapolis, Minnesota

UNTIL recently, little clinical importance was attached to the effects of alveolar carbon dioxide concentrations in excess of 10 per cent. This was true because it was assumed that a reduction in respiratory ventilation sufficient to produce a significant increase in alveolar carbon dioxide tension would produce a much more critical decrease in oxygen tension. In 1926, Van Slyke wrote, "Medical and lay literature contain numerous cases of death from oxygen lack; in respiratory disease, in high altitude, in carbon monoxide poisoning, but it is doubtful that it contains any case of death due primarily to impaired respiratory ability to excrete carbonic acid." Certainly, it is still true that anoxia is of paramount importance in cases of hypoventilation with the patient breathing air; however, there are conditions under which carbon dioxide can accumulate to very high concentrations without concomitant anoxia.

It will be the purpose of this paper to discuss the conditions which are favorable for the development of this situation, to point out certain clinical situations in which these conditions are likely to be encountered, and to mention some of the possible sequelae of severe hypercapnia when it does occur.

Conditions Favoring Carbon Dioxide Retention Without Anoxia

Draper, et al[1,2] have demonstrated that dogs will maintain adequate arterial blood oxygenation for thirty to forty-five minutes in the absence of any respiratory movement if the dogs have breathed 100 per cent oxygen for forty-five minutes prior to the respiratory arrest, and if a patent airway is maintained during the arrest with oxygen as the ambient gas. During this time, alveolar carbon dioxide concentration regularly rises to 40 per cent or higher. They have called this phenomenon "Diffusion Respiration." Under these conditions, oxygen continues to diffuse into the mixed venous blood presented to the pulmonary capillaries since the alveolar oxygen tension is high. However, within the first few seconds of respiratory arrest, the alveolar carbon dioxide tension reaches the level of that in the mixed venous blood. As metabolism continues, the carbon dioxide concentration increases in the tissues, body fluids, and alveolar air practically simultaneously with the major part remaining dissolved in the tissues and blood. Under these conditions, very little of the CO_2 produced is delivered into the lungs because of the low gradient between blood and alveolar air. Since oxygen is being removed from the lungs at its normal rate, the volume of air in the lungs diminishes and more of the ambient gas mixture is drawn into the lungs through the patent airway, replacing in large part the oxygen being absorbed by the blood.

These studies indicate that the conditions favorable for retention of carbon dioxide without anoxia are the following:[3]

1. Inadequate alveolar ventilation.
2. Replacement of the nitrogen of the body with oxygen.
3. High concentration of oxygen in the air available for movement into the lungs.
4. Patent airway.

These conditions are satisfied, partially at least, when a patient has been breathing oxygen, or a mixture containing a high percentage of oxygen, for thirty minutes to an hour and then is subjected to a reduction in respiratory ventilation.

Hypercapnia Under Clinical Conditions

In 1950, Beecher[4] reported studies in which he had made measurements of arterial blood carbon dioxide tension during several types of thoracic surgery. In sixteen patients upon whom pneumonectomies were performed, he found an

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Much of the work reported in this paper was supported by grants from the Minnesota Heart Association and the Graduate School of the University of Minnesota.

TABLE I. SUMMARY OF HIGHEST ALVEOLAR CO_2 VALUES WITH pH CORRELATION DURING FIFTY-THREE MAJOR SURGICAL PROCEDURES

Alveolar CO_2 Level	No. of Cases	Percentage of Total Series	Estimated pH of Arterial Blood
10-15% CO_2	14	26.4	7.16-6.95
15% CO_2 or greater	4	7.5	6.95-or less

be associated with a pH depression to values of 7.16 to 6.95. In 7.5 per cent of the cases, a carbon dioxide level compatible with an arterial pH of 6.95 or lower was observed. These cases were representative of cases from a general surgical service and included laparotomies, thoracotomies, and craniotomies. In most instances, the anesthesiologist was unaware of the

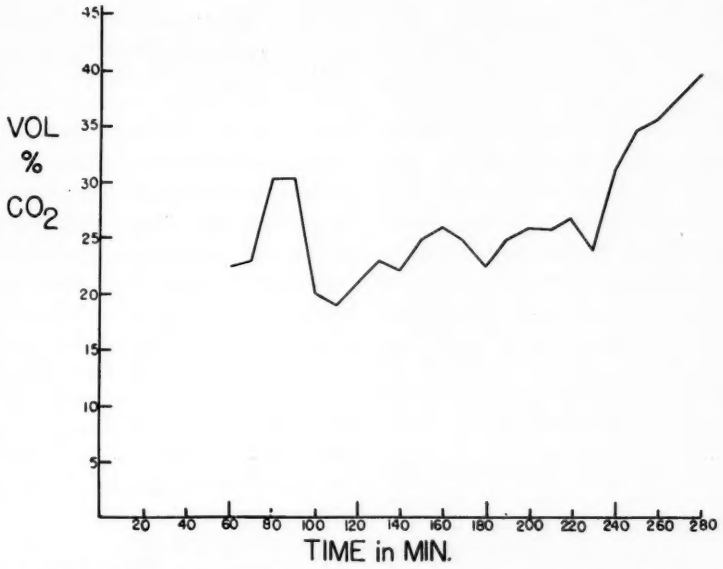

Fig. 1. Alveolar CO_2 levels during pneumonectomy. No recordings were obtained during the first 50 minutes. Despite his knowledge of the mounting CO_2 level, the anesthesiologist was unable to correct the situation with vigorous positive pressure respiratory supplementation. (Reproduced from "Surgical Forum" 1950. By permission of W. B. Saunders Co., Philadelphia).

average alveolar carbon dioxide concentration of 13.7 per cent with an arterial blood pH of 7.09 at some time during the surgery. He stressed position of the patient and the type of surgical procedure being performed as important factors favoring the development of hypercapnia under these conditions. Miller,[5] using a mass spectrometer to record alveolar carbon dioxide concentrations, found elevated tensions in patients undergoing other types of surgery as well as thoracotomies. Table I presents a summary of these data. The pH values in this table are not determined values but are estimated from the CO_2 tensions. It can be seen that 26 per cent of the patients undergoing general anesthetization and major surgery experienced alveolar carbon dioxide concentrations of 10 to 15 per cent during some fifteen-minute period of the operation. We would expect this hypercapnia to state of the carbon dioxide level during the surgery.

In a series of seventeen minor operations performed under cyclopropane anesthesia, Buckley et al[6] found alveolar carbon dioxide concentrations as high as 20 per cent in two patients. The average of the highest levels reached during the operation in this series of patients was 12.3 per cent. None of the patients maintained a normal alveolar carbon dioxide concentration throughout the procedure.

Van Bergen et al[7] have also established that a significant respiratory acidosis is often present in poliomyelitis patients being ventilated artificially while breathing high oxygen mixtures.

Sequelae of Severe Hypercapnia

What are the results of such degrees of hypercapnia? The only clinical evidence of the

presence of this severe respiratory acidosis may be an elevation of blood pressure. However, when the conditions producing the inadequate ventilation are removed and the excess carbon dioxide of the alveolar air and arterial blood is rapidly blown off, profound cardiovascular changes may ensue. It has been demonstrated that dogs will usually tolerate 30 to 40 per cent carbon dioxide in oxygen for four hours or longer with little evidence of cardiovascular damage as evidenced by electrocardiograms and blood pressure.[8] However, when these dogs are returned to air breathing, marked cardiac arrhythmias appear within a few seconds; the blood pressure falls, and ventricular fibrillation and death follow within three to seven minutes in a high percentage of the animals. The only procedures which have thus far been effective in preventing the cardiovascular complications in these animals in our hands are: (1) lowering the inhaled carbon dioxide concentration gradually, (2) maintaining the blood pressure by means of sympathomimetic drugs during the interval of sudden carbon dioxide depression.

Figure 1 demonstrates the hypercapnia that developed during a pneumonectomy for bronchiectasis. The anesthesiologist was unable to prevent this carbon dioxide accumulation even by vigorous manual ventilation. When the patient was removed to the postoperative recovery room a condition suddenly developed which was interpreted as a cardiac arrest; blood pressure was unobtainable, and the heart beat could not be heard. Fortunately, by prompt use of artificial respiration and sympathomimetic drugs, a disaster was prevented, and the patient recovered without further difficulty. While this is the only well-documented instance of clinical post-hypercapnic arrest, a survey of our hospital death files revealed several cases in which this might have been the underlying mechanism. Schumacker and Hampton[9] reported a series of deaths which occurred either during the introduction or removal of the intratracheal tube, a period during which one might suspect that mechanisms similar to the "posthypercapnic phenomenon" were operating.

In his series of patients with hypercapnia during cyclopropane anesthesia, Buckley[6] showed that most of them exhibited an alarming hypotension following the cessation of surgery and anesthesia. This probably merely represents a milder facet of the cardiovascular impairment associated with the "posthypercapnic phenomenon." In fact, Dripps[10] feels that the so-called cyclopropane shock is always a resultant of the associated respiratory acidosis rather than any specific toxic property of cyclopropane. This idea is well substantiated in Buckley's data which showed only two of fifteen patients exhibiting significant hypotension following cyclopropane when adequate respiratory ventilation was carried out and carbon dioxide accumulation was prevented during the period of anesthetization.

Conclusions

Hypercapnia can and does occur clinically in association with conditions of respiratory depression when high oxygen mixtures are utilized to combat the ventilatory deficiency. When such a condition develops it is capable of producing a serious cardiovascular impairment if it is rapidly reversed. The best method of combating this potentially disastrous phenomenon is the assiduous supplementation of respiration so as to prevent the respiratory acidosis from occurring. However, when it does develop the carbon dioxide tension of the alveolar air should be lowered slowly rather than rapidly.

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Acute Pulmonary Edema

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THE currently widespread clinical belief that pulmonary edema is always due to isolated or disproportionate failure of the left ventricle is not actually supported by the experimental studies that purport to confirm it. As was shown elsewhere,[1] the reported work is either inconclusive or else faulty in conception or interpretation. An excellent negative study, that of Meyers et al.,[2] showed that experimentally produced necrosis of the left ventricle causes no increase in pulmonary blood volume. Similarly, the volume has not been consistently found to be increased in patients with cardiac failure generally believed to be due to left-ventricular failure.[3]

There are also certain clinical facts that raise doubts concerning the validity of the left-ventricular-failure theory. Among these facts are: (a) that acute pulmonary edema occurs in chronic cor pulmonale or with pulmonary embolization, (b) that the incidence of the syndrome is much higher with aortic regurgitation than with aortic stenosis, (c) that its incidence is higher in hypertensive crises than in chronic hypertension of similar degree, et cetera. Re-examination of the available clinical and physiologic data should lead to a better understanding of the nature of the syndrome.

Clinical Manifestations

The very beginning of an attack of pulmonary edema is usually not detected or is recognized only in retrospect. When an attack is developing, the patient may have no premonitory sensations; on the other hand, he may first notice a feeling of marked anxiety several minutes (occasionally, several hours) before dyspnea develops. The physician may sometimes misinterpret this anxiety as the cause rather than as the earliest symptom of the attack. Physical examination at such times reveals pallor, an anxious look, and increase in pulse rate and arterial pressure above the patient's normal range; the skin is usually cold and slightly sweaty. The hypertension may be misinterpreted as evidence of a hypertensive crisis that might have caused the attack. It is evident that these signs and symptoms are not specific for pulmonary edema; they can be established as part of the syndrome only if roentgenographic studies show typical areas of haziness close to the hilar regions of the lungs.

The interstitial phase occurs next. In this phase the nonspecific manifestations of the first phase persist, but they are masked by the development of dyspnea, which increases rapidly in severity, and orthopnea, which is usually pronounced. Examination reveals pallor of the skin, now combined with cyanosis. The pulse rate is still accelerated; the arterial pressure either is elevated, as at the onset, or has returned to the patient's normal level. The neck veins may be distended. There is striking prolongation of the expiratory phase of respiration. Wheezing, accompanied by musical râles and rhonchi, is marked in many cases but may be absent in others. Crackling râles are few and inconstant or are absent entirely.

This phase of the attack may last for many minutes or a few hours; on the other hand, the period in which the lungs remain free of detectable intra-alveolar fluid may be so brief as to be unmeasurable. The interstitial phase may proceed abruptly into the phase of alveolar transudation or may be terminated by spontaneous remission or by treatment.

Laboratory studies show rises in hematocrit, erythrocyte count, and hemoglobin level; a lesser rise in plasma protein level may be noted. The circulation time is slowed; a few observations of cardiac output have revealed lowered values for blood flow through the lungs. The vital capacity is lowered markedly, and the arterial blood oxygen saturation may fall to between 70 and 85

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per cent. The right auricular and peripheral venous pressures are elevated, but not necessarily above the upper limit of normal.

The intra-alveolar phase occurs next in patients in whom remission did not occur in the previous phase. The severity of intra-alveolar accumulation of fluid varies markedly; in some patients there is only a little fluid, which is revealed by fine scattered râles, whereas in others bubbling sounds may be audible. The time of onset of this phase varies also; it may occur a few seconds or several hours after the first feeling of anxiety, or in some cases it may not appear at all. The accumulation of fluid in the alveoli and small airways usually aggravates dyspnea and causes coughing. The amount of sputum produced ranges from a few cubic centimeters to a liter or more. Small amounts of mucus, varying quantities of blood, and considerable air are mixed with the plasma that is coughed up.

Examination of such patients shows moderate to marked cyanosis. Tachycardia is present; the arterial pressure is approximately at the patient's usual level. The neck veins are distended. Expiration is prolonged, and crackling or bubbling râles are audible over most of the chest. Wheezing, with its musical râles, may be present also. The crackling and musical râles are not necessarily uniform in distribution; they may be more numerous on one side or over one lobe.

This phase of the attack may be followed by remission—either spontaneous or due to therapy. In many instances, however, shock develops. This too may be either spontaneous or due to the use of tourniquets, positive pressure respiration, or venesection. In a few cases the bubbling râles disappear and the patient reverts to the interstitial phase, with or without wheezing.

Laboratory studies on patients in this state are few and fragmentary. The changes are similar to those described for the interstitial phase but may be more marked.

Shock is common in pulmonary edema. It may be caused by the factor responsible for the edema—myocardial infarction, for example—or may be a consequence of either the pulmonary edema or its treatment.

The development of shock is ushered in by clouding of consciousness in the patient. Although hyperpnea is still evident, dyspnea is not prominent and orthopnea disappears. The pulse rate increases and arterial pressure falls. The veins are narrow and flat. Pallor, grayish cyanosis, and clammy sweating are marked. Examination of the lungs shows signs similar to those of the earlier stages of the attack.

A few measurements of venous pressure have been made in patients with shock associated with pulmonary edema. Values in the normal range occur with mild shock, but very low pressures are found in severe collapse.

The mortality rate is high in patients who have both pulmonary edema and shock. A few patients recover spontaneously; there is no strong evidence that available therapy predictably influences the outcome. The longer the shock persists, the poorer the prognosis.

In the terminal phase deepening of shock, development of coma, and the appearance of cardiac and respiratory arrhythmias indicate impending death.

Basic Physiologic Considerations

The following factors apparently constitute important influences on pulmonary fluid dynamics.

Plasma Protein Level.—There is ample evidence that hypoproteinemia causes increased pulmonary lymphatic flow. No experiments have yet demonstrated that lowered plasma protein level of itself causes overt pulmonary edema. This factor is probably of contributory importance in the pulmonary edema observed in nephritis, cirrhosis of the liver, beri-beri, and some cases of longstanding cardiac decompensation.

Pulmonary Blood Flow.—No experimental study has shown that pulmonary edema is caused solely by increases or decreases in pulmonary blood flow within a reasonable range. On the other hand, there is good evidence that changes in pulmonary blood flow strongly influence the amount of pulmonary edema. Increase in inflow into or decrease of outflow from the lungs aggravates pulmonary edema; changes in the opposite direction ameliorate it. These phenomena are of the greatest importance in clinical pulmonary edema in that they are basic to some of the most effective forms of therapy; tourniquets, venesection, and positive pressure respiration decrease pulmonary inflow, whereas vasodilator drugs increase outflow. In some cases of mitral stenosis, when chronic congestive failure has caused dimi-

nution of flow into and through the lungs, overt attacks of pulmonary edema may cease.

Pulmonary Filtration Pressure.—It is well established that increases in pulmonary capillary pressure aggravate pulmonary edema. However, there is no exact correlation between capillary pressures and the occurrence of the syndrome; this circumstance demonstrates that other factors also are important. Although any rise above the normal capillary pressure causes increased transudation into the tissues, the fluid so filtered does not accumulate unless the rate of transudation is excessive. This excessive rate may be the result of *extremely* high capillary pressure or of a variety of other factors. Increase in capillary pressure is always a contributory cause of pulmonary edema; if extremely large it may be the sole cause. As far as is now known, rises in pulmonary capillary pressure are due solely to rises in pulmonary venous pressure, although pulmonary arteriolar dilation theoretically might have some similar effect. Pulmonary arteriolar constriction tends to lower capillary pressure—or at least minimize its rise. Pulmonary capillary pressure is known to be elevated in three groups of clinical syndromes: chronic congestive failure, mitral valvular disease, and pericarditis. It may possibly be elevated in other diseases.

Pulmonary Venular Pressure. — Pulmonary venular pressure largely determines the pulmonary capillary pressure; the latter must always be slightly higher than the former. Elevation of pulmonary venular pressure by partially ligating the pulmonary veins or inflating balloons in the left auricle causes congestion of the lungs. Detectable pulmonary edema does not develop unless the degree of venous obstruction is extreme—presumably because stasis causes a decrease in pulmonary blood flow.

Other mechanisms of pulmonary venous hypertension that have been revealed by studies in animals are the influence of neurogenic stimuli on the vasomotor system and the effect of histamine on pulmonary venules. These are discussed below.

Available measurements show high pulmonary venous (or left auricular) pressure in patients with mitral disease, and similar—though commonly less marked—changes are found in chronic congestive failure. Their etiologic importance in pulmonary edema is evident. In addition, it is possible that they constitute an important mechanism in the pulmonary edema associated with a variety of intracranial lesions.

Pulmonary Vasomotor Changes.—Increased pulmonary arterial pressure, evidently caused by vasoconstriction at least part of the time, occurs in some forms of experimentally induced pulmonary edema, in anoxia, and during intravenous infusions. This phenomenon may lower the capillary pressure slightly or at least prevent it from rising. More importantly, it causes the right ventricle to expend so much work against pressure that it is unable to increase its output. It is evident, therefore, that pulmonary arteriolar constriction protects the lungs against the development or exacerbation of pulmonary edema. Recent experiments by van Bogaert et al.[4] indicate that this mechanism may operate where pulmonary venous pressure rises. It is not established whether pulmonary arterial hypertension, like peripheral hypertension, depresses the heart and lowers its output through reflex action.

Some types of experimental pulmonary edema —such as that induced by phosgene—are not accompanied by pulmonary arterial hypertension except terminally. Moreover, it is not certain that the observed rises in pulmonary arteriolar pressure in other types of pulmonary edema are entirely due to vasoconstriction—that is, are significantly greater than rises in pulmonary capillary pressures.

It is not yet established that pulmonary venular constriction can be caused by vasomotor activity. Some data obtained in animals with pulmonary edema reveal increases in pulmonary venous pressure that might be due to venoconstriction. Additional fragmentary data pertinent to this problem are to be found in observations that pulmonary capillary pressure may fall after administration of drugs that dilate smooth muscle (i.e., aminophylline) or paralyze autonomic reflexes and thereby presumably dilate pulmonary venules.

Recent work on histaminergic nerve fibers may prove highly important in relation to pulmonary edema. Histamine, normally present in the lungs in a combined form, is freed during the experimental production of pulmonary edema. Epinephrine has this effect; it also increases the blood histamine content. Histamine constricts the pul-

monary venules but not the arterioles, in contradistinction to epinephrine, which constricts both. Acetylcholine resembles histamine in this respect.

The fact that adrenolytic agents inhibit the development of pulmonary edema in animals strongly suggests that vasomotor influences may be important in the precipitation of the syndrome. Many studies of these phenomena must be made before valid conclusions may be drawn.

The pathways that carry vasomotor impulses to the lungs have not yet been delineated. Evidence has been published that the pre-optic hypothalamic nuclei are involved in the production of pulmonary edema in animals, but this work awaits corroboration. The concept that vasomotor centers in the brain may play a role in pulmonary edema raises the possibility that reflexes originating in the viscera and passing through these centers might play a significant role in the development of pulmonary edema. In addition, it is theoretically possible that damage to these centers by infection, hemorrhage, anoxia, or toxins might distort such visceral reflexes, thereby precipitating pulmonary edema, or might cause edema solely through irritation of the centers themselves.

Capillary Permeability.—Currently available methods cannot yield precise data *in vivo* on the physical characteristics of a capillary bed as extensive as that of the lungs. Accordingly, published information on the degree of its permeability to protein in experimental pulmonary edema is based on indirect evidence. The pulmonary edema of experimental alpha-naphthyl-thiourea intoxication and of phosgene inhalation is generally believed to be due to capillary damage. In the case of the latter, available data apparently rule out increased capillary pressure as the chief factor in its production. Burns cause pulmonary edema by damaging capillaries in the lungs. Anoxia also causes increased pulmonary capillary permeability—at least it causes an increased elaboration of fluid in the lungs that is not due to vasomotor changes; a recent study suggests that there may also be some venular constriction in anoxia.[5] At any rate, pulmonary arteriolar constriction, the only vasomotor change definitely shown to occur in anoxia, minimizes tendencies toward formation of pulmonary edema.

Increased capillary permeability seems established as an important causative mechanism in pulmonary edema due to anoxia and to inhalation of toxic gases. Whether it contributes to pulmonary edema in inflammatory lesions of the lungs is a matter of conjecture.

Area of Pulmonary Capillary Filtering Surface.—No data are available concerning how filtration is affected by changes in the area of the total capillary filtering surface in the lungs. It may be taken for granted that filtration is altered by these changes.

Significant increases in pulmonary capillary filtering surface are probably caused by stasis due to high pulmonary venous pressures, as in some of the conditions enumerated above. In addition, increases in total circulating blood volume, as in chronic congestive failure, might have similar effects. It is also possible that blood redistribution resulting from peripheral vasoconstriction in the absence of equal (or any) pulmonary vasoconstriction increases the amount of blood in the lungs and hence also the area of filtering surface. This phenomenon might possibly occur in hypertensive crises or during a febrile reaction; increases in thoracic-duct and cervical-duct lymph flow have been described in animals with fever.

Pulmonary Lymphatic Function.—Experiments in animals have demonstrated that obstruction of pulmonary lymphatic flow aggravates pulmonary edema. One known cause of such obstruction is elevation of pressure in the peripheral venous system, into which all lymphatics ultimately drain. Extensive inflammatory lymphatic thrombosis is almost certainly another cause, but no observations have been published on this phenomenon.

Pulmonary edema in chronic cardiac decompensation is probably aggravated by elevation of peripheral venous pressure, with its secondary consequence of increased pulmonary lymphatic pressure. In addition, inflammatory thrombosis of lymphatics probably contributes to the pulmonary edema encountered in pneumonias—especially those of the interstitial variety.

Bronchial Obstruction.—Several authors have shown that bronchial obstruction accelerates transudation. The mechanism of this change is not known. However, one suggested explanation is based on the fact that forceful inspiration against partial bronchial obstruction increases the negativity of the pressure within the parenchyma—that is, lowers tissue pressure (which ordinarily

resists transudation). Bronchial obstruction causes only a small or moderate increase in extracellular fluid. It is interesting that bronchospasm may be caused by reflexes from the carotid sinuses.

It is possible that the pulmonary edema encountered in some patients with cor pulmonale is partially due to bronchospasm. However, the latter cannot be a potent factor in this respect, since pulmonary edema is rare in other types of bronchial obstruction.

Pulmonary Extracellular Water.—No studies are available on the normal variations in pulmonary extracellular fluid volume; a considerable increase occurs in cardiac decompensation.[6] Even larger increases are grossly evident in pulmonary edema of any origin. It is reasonable to believe that a generalized bodily increase in extracellular fluid favors the development of pulmonary edema to some extent. Extracellular water accumulates in collagenous tissue; it is established that the proportion of collagen to other tissue in the lungs is one of the two highest in the body, being exceeded only by that of collagen to other tissue in the skin.

A generalized increase in body water is found in chronic cardiac decompensation and in some cases of nephritis, malnutrition, and hepatic cirrhosis; this factor probably contributes to the development of pulmonary edema in some patients with these conditions.

Systemic Arterial Hypertension.—Many animal experiments have been made in attempts to study the effects of increased peripheral resistance on pulmonary edema. The procedures used were of several types: ligation of the aorta, administration of epinephrine and related amines, and irritation of the brain. The first group are worthless in the study of the role of the left ventricle in pulmonary edema, since the techniques used also caused marked impairment of cerebral blood flow.

The use of sympathomimetic amines also fails to yield definite conclusions, since resultant increases in left-ventricular work amount to only 100 or 200 per cent—that is, not enough to cause failure of the ventricle. This is shown by the fact that the left ventricle does not fail when its work is increased 1,000 per cent by other means. Some other mechanism must be sought to account for the pulmonary edema caused by these amines. In this regard it is noteworthy that when the same degree of hypertension is experimentally produced by both epinephrine and nor-epinephrine, the latter is found to be less likely to produce pulmonary edema. When it does produce the syndrome, cardiac failure is not the cause.[7] Among those additional effects of sympathomimetic amines that may be important causative factors in pulmonary edema are the pulmonary vasomotor changes induced by these substances and the arrhythmia-producing effect of epinephrine. Moreover, epinephrine causes the release of histamine in the lungs. Theoretical considerations raise another point: it is possible that hypertension conduces to pulmonary edema through reflexes arising within the ventricles that might act on the pulmonary vasomotor mechanisms. The study of reflexes from within the ventricles themselves has only recently begun, many decades after von Bezold first demonstrated them; information on them is fragmentary at present.

The third group of experiments on the relation of peripheral arterial hypertension to pulmonary edema involves the effects of irritation of the brain on peripheral vascular mechanisms. Interpretation of the results of these experiments is impossible because of the simultaneous pulmonary vasomotor changes that occur after the brain has been damaged.

The etiologic role in pulmonary edema of agents or mechanisms that cause peripheral arterial constriction remains to be clarified. It is established, however, that pressor drugs may be given to patients with pulmonary edema without aggravation of that syndrome. Whatever mechanisms are ultimately found, it is clinically evident that hypertension is important in the genesis of pulmonary edema.

Ventricular Damage.—The earlier experiments involving ventricular damage showed that lesions of the left ventricle produced pulmonary edema in animals. Early work also showed that lesions of the right ventricle had the same effect. The more recent work of Meyers et al.[2] showed no increase in pulmonary blood volume after induced necrosis of the left ventricle. Whether myocardial failure occurred in these experiments cannot be ascertained; it is known that the heart cannot be made to fail by any but the most extreme traumatic

damage. In addition, the edema observed in all these experiments cannot be interpreted as due to cardiac failure, since pulmonary edema may occur with experimental lesions of either ventricle. There is as yet no explanation for this edema; reflexes of the von Bezold type, acting on the pulmonary circulation, might account for the experimental results reported. Considerable work remains to be done along these lines.

State of the Respiratory Centers.—Published reports have described the amelioration or prevention of experimental pulmonary edema by means of respiratory depressant drugs; the view has been expressed that the state of the respiratory center may in some way influence the vasomotor mechanisms in the lungs. On the other hand, respiratory depression produced by experimental cerebral damage appears to have no inhibiting effect on the development of pulmonary edema.

The single most useful agent in the control of pulmonary edema in man is morphine; its action in this respect has not yet been explained.

Summary.—Available physiologic data suggest that the pulmonary edema encountered clinically is caused by the summation of submaximal changes in several complexly interrelated physiologic phenomena, with one mechanism or another playing a dominant part in different situations. The fundamental disorder seems to be a rate of transudation from the pulmonary capillaries that exceeds the reabsorptive capacity of the pulmonary lymphatics. The factors that contribute to this imbalance are:

I. Increased transudation
  A. Elevated capillary pressure in lungs
    1. Cardiac decompensation and mitral disease
    2. Venular constriction
      a. Neurogenic
      b. Histamine?
  B. Increased filtering area in lungs
    1. Increased blood volume
    2. Redistribution of blood
      a. Peripheral vasoconstriction
  C. Large blood flow in lungs
  D. Lowered plasma protein level
  E. Increased capillary permeability
    1. Anoxia
    2. Histamine?
    3. Toxins
  F. Bronchospasm
II. Decreased reabsorption
  A. Impaired lymphatic function
    1. Elevated systemic venous pressure
    2. Inflammatory thrombosis?
III. Increased total extracellular fluid volume

Pathologic Physiology

Dyspnea.—The dyspnea that occurs in patients with acute pulmonary edema is caused by several mechanisms. The accumulation of fluid in the interstitial tissues renders the lungs abnormally rigid; hence greater respiratory effort is required. This difficulty involves both inspiration and expiration, but is more pronounced in expiration because of the loss of pulmonary elasticity that occurs. When the lungs become inelastic, expiration necessarily becomes a forcible process instead of one consisting largely of relaxation of the respiratory muscles. Rigidity and inelasticity of the lungs impair mixing, and this circumstance may cause some degree of anoxia. Carbon dioxide is more readily diffusible than oxygen; hence carbon dioxide retention usually does not occur.

The bronchospasm that often occurs in acute pulmonary edema causes dyspnea not only by imposing a need for increased respiratory effort but also by causing anoxia. Lungs in which bronchospasm is present become temporarily emphysematous owing to trapping of air; mixing is accordingly impaired. In severe bronchospasm the amount of air reaching the alveoli may be diminished also.

The accumulation of edema fluid in the alveoli and airways greatly aggravates the anoxia by preventing ingress of air. In addition, trapping of minute air bubbles in the edema fluid results in the formation of a foam that resists expulsion.

Nocturnal Occurrence of Attacks.—The fact that many attacks of pulmonary edema occur at night (or, more accurately, during sleep) has not been completely explained. Several mechanisms that are important in this regard are known, but others may operate.

The circulating blood volume increases during sleep. During waking hours—and more particularly if the patient is up and about—the venous pressure is elevated above the basal level found during sleep, largely as a consequence of muscular activity. The increase in venous pressure, transmitted back to the tissue capillaries, causes the loss of about half a liter of fluid from the circulation into the tissues. The muscular relaxation that occurs during sleep is accompanied by a fall in venous pressure, and the fluid lost returns to the circulation over a period of two or three hours; the plasma volume increases, the

hematocrit falls, and the vital capacity decreases. In effect, the patient gives himself an intravenous infusion during the early hours of sleep; this may precipitate pulmonary edema if a tendency toward the condition is present because of some underlying disease.

Another factor that favors the occurrence of nocturnal attacks is an abnormal vasomotor change that occurs during sleep in patients with congestive heart failure or mitral stenosis. The pulmonary arteriolar vasoconstriction present in these conditions relaxes during sleep; pulmonary blood flow therefore increases, whereas in sleeping normal subjects it decreases. Thus it is evident that the relaxation of the arteriolar constriction removes one of the mechanisms that protect against pulmonary edema.

A third factor is the depression of the respiratory center that occurs during sleep, especially during the earlier hours. Even normal persons show mild or moderate anoxia at such times; patients with impaired pulmonary function probably develop it in more severe degrees. The fact that anoxia causes increased transudation from the pulmonary capillaries is well known.

Fever.—The development of an abnormally elevated temperature is a general indication that heat production exceeds heat dispersal in the body. About five sixths of the heat normally formed in the body is ordinarily dispersed via the skin. Experimental studies in normal persons have shown that diminution of blood flow in the skin is followed after an interval by elevation of the rectal temperature; the cutaneous temperature, of course, falls to or toward that of the ambient air. Cutaneous vasoconstriction occurs regularly during attacks of pulmonary edema; it may be very severe in some cases. In addition, cutaneous flow is slowed, owing to an over-all decrease in cardiac output. It is probable that these phenomena are the cause of the fever that sometimes develops when pulmonary edema persists for many hours.

Shock.—A large amount of blood plasma, containing varying numbers of blood cells, becomes incarcerated in the interstitial tissues of the lungs and is exuded into the alveoli during attacks of pulmonary edema. As much as a liter or more of plasma may be lost from the circulation. Although the shock of acute pulmonary edema is usually due to oligemia, other mechanisms participate in its development. Experiments in animals have shown that severe, protracted anoxia produces shock through some mechanisms not as yet completely characterized. In addition, the shock that occurs in some patients with acute pulmonary edema is due more to the underlying disease—such as myocardial or pulmonary infarction—than to the pulmonary edema itself.

Shock in pulmonary edema may be precipitated by treatment. Morphine may create a tendency toward collapse. Tourniquets, venesection, and positive pressure respiration may also precipitate shock. These procedures are beneficial in pulmonary edema because they decrease the return of blood to the heart; in some instances the fall in cardiac output so induced may precipitate shock in a patient who is already somewhat oligemic and whose cardiac output is low.

Wheezing.—Unilateral novocainization of the vagus nerves in patients with pulmonary edema and wheezes causes the wheezes—but not the crackling rales—to disappear on the side injected. These findings indicate that the wheezing is due to neurogenic bronchospasm. The ultimate origin of the impulses causing the phenomenon is not known.

Spontaneous Remissions.—Nearly all patients suffering from the recurrent type of acute pulmonary edema have spontaneous remission of at least the milder attacks; such remission may also occur in patients who have single attacks of the syndrome in association with conditions such as acute glomerulonephritis, myocardial infarction, hypertensive crises, or acute intracranial lesions. In many instances the remissions are not spontaneous at all, but are due to the patient's accidentally or purposely instituting a therapeutic procedure without medical advice. When a patient with pulmonary edema stands up or sits with feet dependent, the resultant physiologic changes favor amelioration of the edema; these changes are decreased return of blood to the lungs and, after a time, diminution in circulating blood volume.

Another mechanism may also cause spontaneous remissions. The intrapleural pressure probably rises considerably during attacks, owing to loss of pulmonary elasticity and to the increased force and duration of expiratory effort. The return

of blood to the heart and lungs is regulated to an important degree by the intrapleural pressure. Loss of the normal negative pressure impedes the venous return; therefore the attack itself causes changes that favor cessation of the attack. Obviously the circulatory changes so induced are not always great enough to cause remission.

Patients who cough up large amounts of sputum during an attack are, in effect, performing a venesection on themselves. This tends to diminish the severity of the attack, although some patients die despite the benefit of this physiologic phenomenon.

Treatment

Morphine, oxygen, aminophylline (by vein), tourniquets, and venesection constitute the traditional therapy of individual attacks. To these have recently been added anti-foaming agents and ganglion-paralyzing drugs. Hilden[8] has recently reported good results with tetraethyl ammonium bromide, and Wilson[9] has found hexamethonium effective. These drugs should, of course, be used with great caution. Digitalis, salt restriction, and mercurial diuretics serve better in the prevention of recurrent attacks of pulmonary edema in patients with chronic cardiac decompensation than in the treatment of the attacks themselves. Acute hypertensive crises accompanied by pulmonary edema are usually relieved by the injection of veratrum derivatives.

The use of the therapeutic measures discussed here is commonly attended by remission of the syndrome. However, a disappointingly large number of patients fail to respond satisfactorily. Because knowledge of the disorder is still incomplete, its treatment requires close observation of the patient, understanding of the mechanisms of therapy, and avoidance of rigid routines—especially those based on *a priori* theories.

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FACTS ABOUT "MIKE SHOT" OF "OPERATION IVY"

1. It was a ground test of a thermonuclear device, not a bomb dropped from the air.
2. It took place at Eniwetok Atoll in the Pacific in November, 1952.
3. The fireball measured 3¼ miles in *diameter*.
4. The *radius* of total destruction was 3 miles.
5. The *radius* of heavy to medium damage was 7 miles.
6. The *radius* of light damage was 10 miles.
7. The blast destroyed the tiny island of Elugelab, leaving a crater roughly 1 mile in diameter and 175 feet deep at the deepest part.
8. After twelve minutes, the cloud was nearly 20 miles high and 100 miles across.
9. Some damage from any similar device would be suffered over an area of somewhat more than 300 square miles—about the area of metropolitan New York City . . . *but*
10. Complete destruction would cover less than 30 square miles—1/100,000th of the surface area of the continental United States.—*Federal Civil Defense Administration.*

Idiopathic Pleural Effusion

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THE ACCUMULATION of fluid in the pleural cavity is a complication of many conditions. In most of these, such as heart disease, renal disease, obvious pulmonary tuberculosis or an acute pneumonic process, careful study will reveal the cause of the effusion. Hydrothorax due to an intrathoracic malignant tumor, pulmonary infarct, subdiaphragmatic disease or lymphoma may be more difficult to recognize but a definite etiologic diagnosis can usually be made. However, effusions may arise without any of these causative factors being present, and these have been called "idiopathic pleural effusions." Experience has shown that they are usually tuberculous and that the physician's responsibility to the patient demands that he regard and treat them as such unless they can be proven to be due to other causes. This conclusion is based on four observations:

1. The tuberculin reaction in patients with idiopathic effusion is almost invariably positive although in normal members of the same age group the positive reaction rate is low.

2. Special studies show tubercle bacilli in the pleural fluid in up to 70 per cent of these patients although routine cultures for tubercle bacilli are positive in only 25 to 30 per cent.

3. Pathologic studies have shown definite tuberculous lesions in the pleuras of such patients.

4. Active pulmonary tuberculosis occurs within five years after such an effusion in from 20 to 60 per cent of reported cases.

Pathogenesis

In young adults, the majority of pleural effusions are of this "idiopathic" type.[1] However, with increasing age, the picture changes so that in patients over the age of fifty, carcinoma and congestive heart failure become the two most common causes of fluid in the chest.[2] Lloyd[3] recently reported the thoracoscopic findings in twenty-three patients with hydrothorax and found malignant tumors producing the fluid in seventeen. He did not, however, give evidence that these effusions were actually "idiopathic" before the thoracoscopic studies, nor did he state the age or tuberculin reaction of his patients.

The pathogenesis of pleural effusion in tuberculosis has been a matter of speculation in much of the recent literature on the subject. Mention has been made of the possibility of a subpleural focus of tuberculous infection involving the pleura either by lymphatic drainage or by direct extension. Caseous mediastinal lymph nodes have also been suggested as the source of the infection, and the possibility of hematogenous spread to the pleura has been proposed.[4-8] However, until recently no good anatomic evidence has been advanced to support any of these theories.

Stead and his co-workers,[9] in a recent study, have done much to clarify this problem and to improve our understanding of the mechanism by which these effusions arise. They reported a series of fifteen patients with tuberculous pleurisy who underwent thoracotomy within a few months of their acute effusions. In each case, they found a chronic granulomatous pleuritis with complete obliteration of the pleural space. Typical caseous tubercles were seen within the thick fibrous peel which encased the lung; and in twelve of the fifteen, acid-fast bacilli were seen in the stained sections.

On examination of the underlying lung, they found in twelve of their cases a caseous tuberculous focus immediately beneath the pleura at which point the peel was so intimately attached to the lung that decortication was impossible without removal of the parenchymal lesion. In the other three cases tuberculous foci were also present within the lung, but the source of pleural contamination was not identified. They postulated that the site of rupture of the parenchymal

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lesion might have been buried in one of the interlobar fissures.

These authors also called attention to some significant articles in the literature which had received little attention previously. These earlier papers described the thoracoscopic appearance of the infected pleura and the results of autopsies performed on several patients with acute idiopathic effusions. Definite tuberculous lesions were regularly found in the lungs at autopsy, and the thoracoscopic appearance in the acute cases was typical of tuberculosis.

The significance of these findings can readily be appreciated in the light of Paterson's work on the experimental production of tuberculous pleural effusion in guinea pigs.[10] The injection of tubercle bacilli into the pleural cavity of a tuberculin-sensitive guinea pig produced a vigorous pleural reaction and an effusion which were followed by a fibrinous pleurisy. A similar intrapleural inoculation in a tuberculin-negative animal resulted in very little pleural reaction but a much higher incidence of disseminated tuberculosis.

The lesions which they saw at surgery plus the experiments of Paterson led Stead and his co-workers to the conclusion that tuberculous effusion is caused by the rupture of a subpleural parenchymal caseous focus into the pleural space. This discharge of infected material into the pleural space of a tuberculin-positive subject results in an actual infection and a vigorous inflammatory reaction of the membrane. This concept was supported by their finding of tubercle bacilli in caseous lesions within the thickened pleura. The possibility still remains that in a few cases effusions may arise by hematogenous seeding of the pleura, especially in those occasional instances where the effiusion is bilateral. There seems to be little doubt, however, that most arise by the sequence of events which they describe.

Clinical Picture

As stated previously, idiopathic pleural effusion is primarily a disease of young adults. The peak incidence is at about age twenty, about ten to twelve years earlier than the peak incidence of pulmonary tuberculosis.[4,11] The fact that many of these effusions occur within a few months of the conversion of the tuberculin reaction is evidence that effusion may frequently be a complication of a primary tuberculous lesion in young adults who have escaped such a primary infection in childhood. In contrast to this is the unexplained observation that pleural effusion rarely develops in children with primary tuberculosis. Primary tuberculosis in the adult is uncommonly associated with enlarged hilar nodes on x-ray.

The clinical picture accompanying an effusion varies widely. There may be an actue fulminating onset with high fever, chest pain, cough and dyspnea, or the patient may be totally asymptomatic and his effusion discovered on a routine chest x-ay. In the majority of cases the disease begins with a mild to moderate chest pain, fever up to 103 degrees, and a slight irritative cough. An acute onset may suggest a bacterial pneumonia, but this can usually be recognized by the clinical picture and bacteriologic findings.

The usual physical findings of dullness and decreased or absent breath sounds and fremitus are well known, but Bernstein and White[12] have called attention to the frequency with which the physical examination may be atypical. They described seventeen patients with pleural effusion of whom eight also had signs of pulmonary consolidation. They postulated that these findings were caused by compression of the underlying lung by massive effusion.

Routine laboratory findings are those of a chronic inflammatory process. Mild leucocytosis may occur but the leucocyte count is usually normal. The sedimentation rate is usaully elevated and correlates roughly with the vigor of the pleural reaction. The pleural fluid is an exudate, usually yellow-amber in color, and may be clear or cloudy. The specific gravity is usually between 1.015 and 1.020 with a protein content of approximately 3 to 5 gm. per 100 ml. Bloody fluid is rare in the white race, but may occur in 2 to 3 per cent of cases. The cells of the exudate are chiefly mononuclear although neutrophils may be present in an early effusion. It has been shown recently that fluids from which tubercle bacilli can be isolated contain significantly less glucose than do fluids from patients with non-tuberculous effusions. However, the usefulness of this procedure is limited by the fact that sterile, truly idiopathic effusions show a sugar content in an intermediate, equivocal range.[13,14]

Careful bacteriologic study of the pleural fluid will result in demonstration of tubercle bacilli in

only 25 to 30 per cent of cases. Success with routine cultures alone will be considerably less than this, and all such fluids should be inoculated into guinea pigs as well. Repeated attempts will increase the percentage of positives; and it has been suggested that, in cases where the effusion is large, the laboratory be provided with a large volume specimen which can be centrifuged before culture and guinea pig inoculation.[1,4,5,16]

The tuberculin test is of great help as it must either be positive at the time of onset or become so within six to eight weeks, or the diagnosis of tuberculosis can be virtually ruled out. On the other hand, if a history of a previously negative Mantoux can be obtained and an effusion appears coincidentally with conversion to positive, the tuberculous etiology is well established. Roper and Waring[15] found 100 per cent tuberculin reactivity in 141 cases of primary pleural effusion despite the fact that a Mantoux history was usually not obtainable at the time the cases were selected for their series. Oille[1] reported eight of seventy-eight patients Mantoux-negative at first testing, but these all became positive within two months. Kraft[16] described 100 cases in which seventy-seven of the patients reacted to PPD No. 1 and the remaining twenty-three to PPD No. 2.

Since pleural effusion arises from underlying pulmonary tuberculosis, it is also important that bacteriologic study of sputum and gastric washings be done. Mitchell[21] obtained a higher incidence of positive cultures from sputa and gastric washings than from the pleural fluid even though no parenchymal lesions were noted on x-ray.

Lloyd[3] used thoracoscopy and pleural biopsy in cases of pleural effusion where a diagnosis was impossible by other means and found it a safe procedure. He reported no serious adverse effects in twenty-three cases where thoracoscopy and biopsy were done after preliminary aspiration and introduction of air.

Therapy

The therapy of idiopathic effusion may be divided into two aspects: the treatment of the effusion itself and that of the underlying tuberculous process.

The policy as to management of the fluid varies widely in different series. Most authors agree that at least one thoracentesis should be done for diagnostic purposes, but some restrict further aspiration to those instances where the effusion is productive of dyspnea or where the fluid fails to re-absorb in a reasonable time.[1,7] Sibley[5] demonstrated that the incidence of later morbidity and mortality was not affected by aspirations. However, it has been shown that persisting fluid may rapidly result in marked fibrin deposition, pleural thickening, and loss of lung function. This has caused some authors to recommend regular and systematic removal of fluid at least down to the level of the dome of the diaphragm, despite the absence of proof that this favorably effects the incidence of later pleural complications.[4,17,18,19] In the older literature, introduction of air to create an artificial pneumothorax was recommended in an attempt to maintain a free pleural space, but this is now felt to be contraindicated.[6]

Therapy after resolution of the effusion is directed at the underlying tuberculosis. In addition to the subpleural tuberculous foci which gave rise to the effusion, Stead et al[9] found in seven of their cases multiple caseous lesions scattered through the lung. Despite the fact that these were extensive enough to be classed as moderately advanced or far advanced at the time of surgery, they were either unsuspected or their extent was not fully appreciated on preoperative x-rays. This finding, plus the high incidence of subsequent tuberculosis, makes it imperative that these patients receive the same treatment ordinarily advised for a demonstrable pulmonary tuberculosis.

Six months of bed rest is usually recommended after the effusion has disappeared or the fibrotic pleura has become stable on x-ray. This period is followed by four to five months of gradual ambulation, which results in a total of approximately one year in the sanatorium. Roper and Waring showed a reinfection rate of 86 per cent in their patients treated with less than six months of rest, 34 per cent in those treated six months to a year, and only 13 per cent in those with over one year of therapy.[20] Falk and Tucker[22] found found an 8 per cent tuberculous complication rate in patients hospitalized eight to sixteen months as compared with 21 per cent in the group treated less than eight months.

Although less emphasis is being placed on bed rest in the treatment of tuberculosis, it should be stressed that this modification of treatment is still experimental. Most physicians experienced in tuberculosis believe that rest is a very important

part of the treatment of tuberculosis. This also applies to pleurisy with effusion since it is simply a manifestation of tuberculosis. Antimicrobial therapy should be used in conjunction with systemic rest in the same manner that it is employed in other forms of pulmonary tuberculosis.

Since the etiology of the pleurisy can be established bacteriologically only in a minority of instances, it may tax the ingenuity of the physician to convince the patient of the need for prolonged hospitalization. This difficulty is further increased by the fact that the fluid usually disappears rather rapidly and the patient frequently feels quite well within a few weeks. Only a physician who is convinced of the tuberculous etiology and the serious significance of such an effusion can sell such a program to the patient.

Prognosis

Frostad[11] reported that 26.4 per cent of patients admitted for tuberculosis gave a history of pleural effusion as the first sign of their disease. Falk and Tucker[22] found a history of previous effusion in 8 per cent of 250 consecutive patients admitted to the hospital for pulmonary tuberculosis, while in patients with skeletal and genito-urinary tuberculosis, they obtained a similar history in 37 per cent and 23 per cent, respectively. These figures again demonstrate the importance of pleural effusions as a precursor of later, more serious, tuberculous infection.

Age seems to be a factor as Falk and Tucker found all of their subsequent relapses occurred in the age group thirty or under. They also showed that non-white patients showed a significantly higher incidence of later tuberculosis, an observation confirmed by Bonilla[8] and by Jones and Dooley.[23] The later authors also found specifically that the subsequent occurrence of extrapulmonary disease was higher in the Negro.

The demonstration of tubercle bacilli in the pleural fluid has been shown by several authors to have little effect on the total number of patients who subsequently develop tuberculosis.[1,5,11,21,22] However, there seems to be a higher incidence of extrapulmonary disease in those patients with positive pleural fluid[22] and also in those bilateral effusions.[7]

Several authors mention the frequent occurrence of extrapulmonary tuberculosis after pleural effusion, the incidence varying between 5 and 25 per cent.[5,8,11,22,23] This indicates that tuberculous bacteremia commonly accompanies tuberculous pleurisy and is probably due to the widespread lymph drainage of the infected pleura. Burke[24] has studied the fate of particulate matter injected into the pleural cavity and has shown that the usual drainage is into the parasternal, para-aortic, and paravertebral nodes. His autopsy data indicate frequent involvement of these nodes in tuberculosis of the chest wall and of the spine following effusion. He has demonstrated the importance of the paravertebral nodes in the pathogenesis of Pott's disease.

The size of the effusion seemed to have little effect on the ultimate development of tuberculosis.[11] However, the presence of a demonstrable pulmonary infiltrate on x-ray was accompanied by a significantly higher morbidity rate.[8] This is probably because in patients with progressive infection demonstrable pulmonary infiltrates tend to develop during the period of observation.

Clinical spread generally becomes manifest within two years of the effusion. Falk and Tucker[22] found that the acute hematogenous complications (miliary, meningeal and peritoneal) occurred within an average of one year after effusion. Comparable average figures for the time of onset of pulmonary, skeletal and genito-urinary tuberculosis were 1.64, 1.85 and 2.57 years, respectively. Frostad[11] found 80 per cent of the morbidity and 84 per cent of the mortality in his patients occurred within five years after the effusion. Mitchell[21] found 93 per cent of recurrences by the end of the fifth year. Frostad quotes Norweign life insurance studies which show that in patients followed for four years after effusion, the mortality from tuberculosis is four times that of the general population. All of these figures tend to emphasize the potential seriousness of this condition and the need, not only for adequate treatment at the time of diagnosis, but also for close follow-up for at least five years.

Summary

1. Many pleural effusions, especially in young adults, arise without an obvious etiology. The evidence for a tuberculous etiology for such effusions is reviewed. "Idiopathic" pleural effusions must be recognized and treated as tuberculosis if the patient is to avoid the danger of subsequent tuberculous complications.

2. Careful laboratory studies, including skin testing and culture and guinea pig inoculation of

pleural fluid, sputum and gastric contents, will frequently point to tuberculosis as the etiology. However, many such effusions never show positive bacteriologic studies, and a negative result does not rule out tuberculosis.

3. Treatment consists of aspiration of all readily obtainable fluid, anti-tuberculous chemotherapy, and bed rest, until the x-ray picture has been stable for at least six months. Patient acceptance of this regimen is dependent on a positive attitude on the part of the physician.

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FARM-CITY WEEK, OCTOBER 23-29, 1955

Each physician and his medical society is invited to plan and participate actively in Farm-City Week, October 23-29, a week-long series of events aimed at bringing about better understanding between rural and urban dwellers.

Under the sponsorship of the Farm-City Conference, an informal alliance of leaders in industry, agriculture, and the professions, Farm-City Week is hoped to be one of the most effective ventures in good citizenship ever undertaken. Member organizations, representing several million people, are going "all out" to make the week national in scope through observances in every community across the country.

The AMA, a conference member, has already sent program plans and suggestions to all medical society officers. Kiwanis International has been selected as the co-ordinating agency, and local Kiwanis club officers have been informed of the invitation to participate in state and community programs.

Because Farm-City Week provides a splendid opportunity for the medical society to assert its civic leadership and to inform the public of its many services, the AMA urges all physicians and societies to get behind this program to help dramatize the mutual need for good relationships between town and country neighbors.

Health and medical care are of uppermost interest in this activity dedicated to urban and rural progress. Medical societies can add greatly to the success of the week by developing health programs for city and farm groups, addressing civic organizations, participating in newspaper, radio and TV interviews, providing tours of medical facilities, and presenting vocational guidance programs in secondary schools. In addition, physicians, as members of the community, should be represented in the general observances of Farm-City Week.

A successful Farm-City Week, October 23-29, depends upon community-wide action. The medical profession—both as individual members and as a professional unit—should accept this challenge.

Individual Contributions

Radioisotope Studies of the Physiology of Calcified Tissues

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ON casual view the bones give an impression of rigidity and permanence which belies their dynamic physiology. Prior to the work of Hevesy, who demonstrated[1] about two decades ago, shortly after radiophosphorus first became available, an unexpectedly large and rapid incorporation of this radioisotope in the skeleton, it had been assumed that the bone mineral is resorbed and deposited only as a result of changes in the ionic concentration of the body fluids or of the activity of the osteoblasts and osteoclasts. The studies with radioisotopes have demonstrated that the bone mineral is not a static stone but is a dynamic system in which the elements are constantly turned over and renewed. Because of the rapidity and extent of these processes the skeletal minerals are intimately associated with all other aspects of the transport and metabolism of these elements. The deductions which have been made from the studies with radioisotopes have pointed out an important physiological concept, namely, that the skeleton has a homeostatic function in maintaining and regulating the ionic composition of body fluids which is fundamentally more important than its role as a supporting tissue.

An example of a research which is frequently cited to indicate the high order of rate of turnover of skeletal phosphorus is the work reported by Hevesy, Levi and Rebbe.[2] These workers maintained what was stated to be a constant specific activity of plasma inorganic phosphorus of rabbits over a period of several weeks by spacing of repeated intravenous injections of radiophosphorus as inorganic phosphate. The specific activity* of the bone phosphorus as a percentage of the specific activity of the plasma inorganic phosphorus gave the results in Table I which denote the fractions of the phosphorus in the bones which were renewed in fifty days. For example, about one-fourth of the phosphorus of the femur and tibia epiphyses was replaced in fifty days. Smaller fractions of the phosphorus of long bone diaphyses were replaced but even in this case the quantity of phosphorus involved is considerable.

TABLE I. EXTENT OF REJUVENATION OF RABBIT BONES

	Phosphorus Replaced
In 50 Days	Per Cent
Femur epiphysis	29.7
Femur diaphysis	6.7
Tibia epiphysis	28.6
Tibia diaphysis	7.6
Ribs	27.5
Scapula	43.8
Incisor dentin (root)	103.0

It is not correct to conclude that bone mineral is dissolved, removed and replaced with newly deposited bone mineral through the operation of the biological processes of bone resorption and bone formation in order to account for the degree of turnover of the bone mineral which is demonstrated by the accumulation of radioisotopes in the skeleton. The mechanism in largest part is one in which the labeled ions, for example phosphate, in the body fluids exchange for and replace an equal number of unlabeled ions in the bone salt. This concept was legitimately drawn by inference from the whole animal experiments but the direct evidence for this conclusion was first obtained from experiments carried out *in vitro*. It was shown that dead calcified tissues rapidly remove large amounts of radiophosphorus from solution without affecting the total concentration of phosphate ion in the solution.[3]

*Specific activity=fraction of injected radioisotope per milligram of the element.

Presented before the Minnesota Academy of Medicine, November 10, 1954.

TABLE II. TURNOVER OF PLASMA CALCIUM AND SODIUM

	C_o C/M/ml.	R_p %
6 animals		
Ca	1184	51.9
Animal No. 14		
Ca	1046	60.1
Na	933	56.4
Animal No. 15		
Ca	613	30.3
Na	586	29.7
Composite of Animals 14 and 15		
Ca	758	38.8
Na	750	43.9

The rate of turnover of skeletal calcium and sodium can be estimated in the living animal without the necessity of maintaining the plasma specific activity constant by following the rate of dilution in the blood of intravenously injected radioisotopes of these ions. This procedure is applicable only to those inorganic ions which are located solely or mainly in bone mineral and extracellular fluid. This method cannot, therefore, be used to measure the rate of turnover of skeletal phosphorus or potassium.

In our experiments[4] dogs received a rapid intravenous injection of a solution containing calcium[45] or both calcium[45] and sodium[22]. Arterial blood samples were obtained, beginning one minute after the injection and at frequent intervals thereafter, from a cannula which had been inserted into the femoral artery (Fig. 1). The concentration of each of the isotopes in the arterial plasma samples was determined and the results are shown by the points on the curves in Figure 1. The concentration of the radioisotopes in the plasma fell rapidly; that of calcium more rapidly than that of sodium and the concentration of radiocalcium continued to fall long after an equilibrium concentration of radiosodium in the plasma had been reached. Obviously equal numbers of the ions must move simultaneously in both directions between adjacent compartments since the concentrations of each of the ions in plasma and interstitial fluid are held constant. The concentrations of the radioisotopes in the plasma fell because of the movement of the labeled ions from plasma to interstitial fluid and from interstitial fluid to bone. The labeled ions in the fluid compartments were thus replaced with a similar number of unlabeled ions.

Equations in three exponential terms for sodium and four exponential terms for calcium were derived from the data to describe the time-concentration curves for each isotope in plasma. The curves shown in Figure 1 are actually the plots of the equations. The success of the curve fitting is shown by the agreement of the observed values, indicated by the points, to the curves.

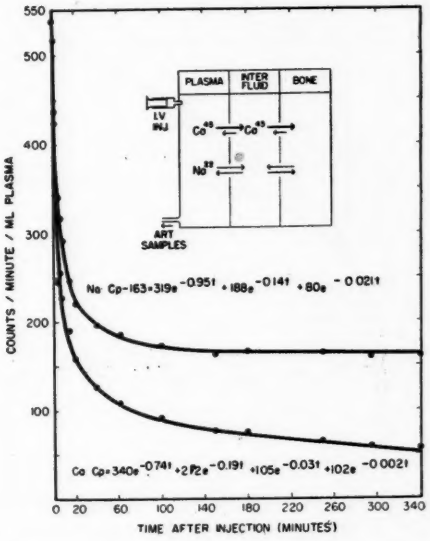

Fig. 1. Diagram of experiment and results showing rates of disappearance of intravenously injected radioisotopes of calcium and sodium.

At any actual time the number of labeled ions in the plasma is determined by the number which have left the plasma and the number which have returned to the plasma. At zero time there are no labeled ions in the interstitial fluid and the change in concentration of the labeled ions at zero time is thus determined only by the number which are transported from plasma to interstitial fluid.

The sum of the first derivatives of the exponential terms in each equation at zero time gives the instantaneous rate of change of the number of labeled ions in the plasma at that time. In effect one obtains by this mathematical device the number of labeled ions which leave the plasma per unit time before any have left. If this number is then divided by the number of labeled ions present in the plasma at zero time the fraction of labeled ions transferred across the vascular membrane per minute is obtained. Since we can assume identical behavior of the labeled and non-labeled ions, this fraction is then identical with the fraction of ordinary plasma calcium and ordinary sodium transferred across

the capillary membrane in both directions per minute.

The results as to transcapillary migration rates of calcium and sodium are given in Table II. The

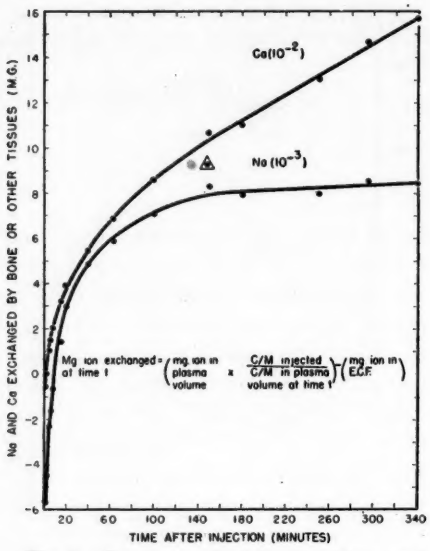

Fig. 2. Turnover of skeletal calcium and sodium in dogs.

averaged results obtained with six animals indicate a turnover and replacement from the interstitial fluid of 52 per cent of the plasma calcium per minute. From the two animals which received both radioisotopes, the not unexpected result of equal rates of transcapillary transport of sodium and calcium was obtained.

As was seen, the intravenously injected radiocalcium and radiosodium in the plasma rapidly became diluted in quantities of calcium and sodium which far exceeded the amounts of these ions present in the extracellular fluid compartments. By use of the isotope dilution equation the data given in Figure 1 were also used to estimate the quantities of skeletal calcium and sodium exchanged at each of the time intervals. It is assumed, upon sound grounds, that bone is the only tissue which can supply significant quantities of calcium or sodium ions to extracellular fluid.

In the equation as used (Fig. 2) the first step was to calculate the total quantity of sodium or calcium through which the injected isotopes were distributed in order to give the observed activity per milligram of each element in the extracellular fluid as sampled by the plasma. The first two terms in the equation gave this result. From this quantity was subtracted the amount of calcium or sodium in extracellular fluid to give the amounts of these elements which had been exchanged by bone at each of the time intervals after the injection.

This equation requires that it be assumed that the specific activity of each labeled ion is equal in plasma and in interstitial fluid at any given time. This assumption is incorrect over the very early minutes after the injection but the error thereby introduced rapidly decreases with time. Certainly by 150 minutes the calculated quantities of exchanged bone calcium and sodium are liable to only a small error.

The results show (Fig. 2) that by 150 minutes the skeleton of a 20 kg. dog had exchanged about 1 gram of calcium and about 8.2 grams of sodium. Both of these quantities are large and indicate that significant amounts of bone mineral calcium and sodium are delivered to the fluid compartments of the body in short periods of time. The quantity of sodium is of the order of half of the entire amount present in the skeleton. The very rapid turnover of skeletal sodium, compared to the slower rate of turnover of skeletal calcium, is consistent with the Hendricks-Hill description[5] of the location of bone sodium as adsorbed ions on the bone mineral crystals.

Through studies with radioisotopes a continual remodeling of bone as a whole and of its mineral phase can be demonstrated. The remodeling occurs by formation and maturation of Haversian systems[6] and by recrystallization of the bone mineral.[7,8] One line of evidence for *in vivo* remodeling of bone, which is at the same time an expression of the result of the remodeling, is the gradual sequestration of originally labile and freely exchangeable radiocalcium into situations in the bone which are remote from the body fluids.

In our experiments[9] radiocalcium was given to mature rats by intraperitoneal injections and the animals were sacrificed at periods of time from one day to 210 days after the administration of the radioisotope. The fractions of the injected radiocalcium present in the entire skeletons of the animals were determined and these results are shown by the heavy descending line in Figure 3. At Day 1 80 per cent of the injected radiocalcium was present in the skeleton. This quantity de-

creased because of mobilization of the labile skeletal radiocalcium and its excretion until the fiftieth day when about 45 per cent of the injected radiocalcium was still present in the skeleton. After this time there was no further significant decline in the amount of radiocalcium retained in the skeleton. These results indicate that processes of bone remodeling and of bone salt recrystallization which had occurred over the first fifty days had resulted in the relocation of a considerable fraction of the radiocalcium in locations which were inaccessible to the body fluids.

Another constituent of bone mineral which exhibits a rapid rate of turnover is the bone inorganic carbon. Our studies show that the biological half-life of bone inorganic carbon in growing rats is twelve to fifteen days and in mature rats is about thirty to forty days.[10]

A variety of methods have been used to administer radioactive carbondioxide to animals and to build up and maintain the radiocarbon label of body fluid inorganic carbon. In one phase of our work this result was obtained by the continuous intraperitoneal injection of sodium carbonate labeled with radioactive carbon. In one experiment a large rat received sodium carbonate in this manner by injection over a period of 116 hours.[11] When this animal was sacrificed, radiocarbon was found in every tissue examined, and some results are given in Table III. The skeleton as a whole had accumulated about 0.1 per cent of the injected radiocarbon. Since the specific activity of the bone inorganic carbon was higher than that of any other tissue carbon, this carbon had the highest rate of turnover of any fixed carbon in the body. The incisor teeth inorganic carbon is a special case due to the fact that radiocarbon was accumulated by deposition consequent upon growth of the teeth as well as by exchange.

Our knowledge of the physiology of the teeth has been notably advanced through studies with radiotracers. The old question of the permeability of enamel and dentin has been answered by the demonstration of a two-way transport of labeled ions and some molecules through these dental hard tissues.

When radioisotopes of phosphorus and calcium are given to experimental animals by injection or by stomach tube,[12] these isotopes can be found in the enamel and dentin. Dentin acquires much smaller amounts of these mineral isotopes than bone and the specific activity of enamel is, in different experiments, of the order of 5 to 20 per cent that of dentin as is shown in Table IV. Whether the avenue of entrance of labeled iso-

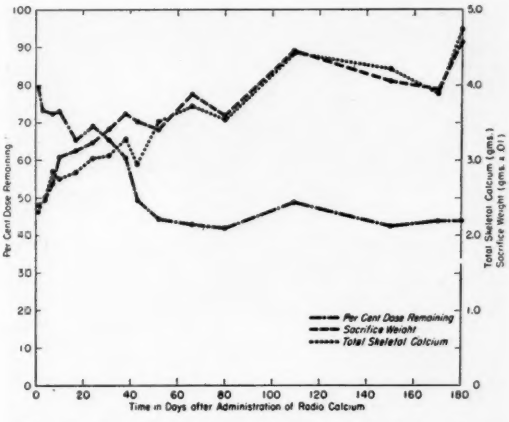
Per Cent Dose Remaining
Sacrifice Weight
Total Skeletal Calcium
Per Cent Dose Remaining
Total Skeletal Calcium (gms.)
Sacrifice Weight (gms. x .01)
Time in Days after Administration of Radio Calcium

Fig. 3. Retention of radiocalcium by skeleton of rats.

TABLE III. DISTRIBUTION IN TISSUES AND TISSUE COMPONENTS OF RADIOACTIVE CARBON FOLLOWING CONTINUOUS INTRAPERITONEAL INJECTION AS SODIUM CARBONATE

Tissue or Tissue Component	Fraction of Total Dose Per Cent	Specific Activity x 10^4	Relative Specific Activity (Bone Inorg. Carbon = 100)
Bone Inorg. C		715.4 ± 6.25	100.0
Bone	0.1162 ± 0.0006	90.0 ± 0.46	12.6
Bone Protein		25.5 ± 0.41	3.6
Incisor Teeth	0.0016 ± 0.00002	76.9 ± 0.82	10.7
Incisor Teeth Inorg. C.		1138.9 ± 5.3	159.2
Molar Teeth	0.0008 ± 0.00001	51.5 ± 0.68	7.2

TABLE IV. RADIOISOTOPE UPTAKE BY CALCIFIED TISSUES (RAT—5 DAYS AFTER INJECTION OF CA^{45} AND P^{32})

	Relative Specific Activity P^{32}	Ca^{45}
Femur epiphyses	80	92
Femur diaphyses	75	82
Molar dentin	14	12
Molar enamel	2.7	1.2

topes into the enamel is from the blood *via* the dentin or from the saliva has been debated. The best evidence is that both avenues are open and operating. In the case of radiocalcium and radiophosphorus it appears that the transport from saliva to enamel is relatively the more important. The migration of ions and molecules through the surface of the enamel and into the teeth can be demonstrated in simple *in vitro* experiments in which the crowns of extracted teeth are immersed in solutions of the radioisotope.

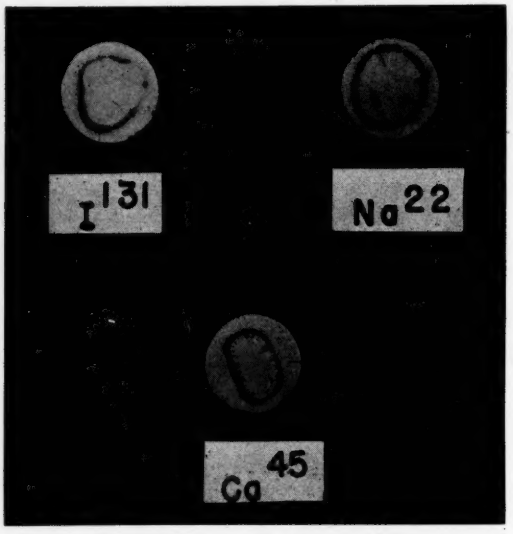

Fig. 4. Radioautographs showing migration of radioisotopes into the enamel of human teeth.

The radioautographs in Figure 4 were prepared from human teeth whose crowns had been immersed in the solutions of the indicated radioisotopes. The migration of these ions into the enamel is evident. These and other studies of the centripetal migration of ions which are part of the enamel mineral indicate that exchange of ions between the enamel and saliva is a normal physiological process.

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BATTLE AGAINST TUBERCULOSIS STILL CONTINUES

One fact which must be acknowledged and is of practical importance is that over the country the annual number of newly reported cases of tuberculosis has declined very little. In fact, the number increased from 1940 until 1948 and, while it has gone down for the past four years, in 1952 it was still slightly higher than in 1940, although the case rate has gone down since it is affected also by the increasing population.

Even though many of these patients do not require hospitalization, all should be investigated, their clinical status determined, their familial contacts studied and other appropriate control measures taken where indicated.

Thus, there has been no decrease in the effort required of health departments and voluntary agencies, and no reduction in personnel or funds should be contemplated. In fact, greater effort is demanded if tuberculosis is to be eradicated, and no lesser goal should satisfy us.—PHILIP E. SARTWELL, M.D., *Nat. Tuberc. A. Tr.*, May, 1954.

Influence of Anesthesia on Maternal Mortality

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THE majority of pregnant women who come to delivery are young, healthy, vigorous patients. Most of them have been watched carefully throughout their prenatal course. A good history and physical examination have been taken, which will aid the person giving the anesthesia to give that type of anesthetic which will be the easiest for the mother and the baby and yet will be the safest. Therefore, the calculated risk of anesthesia for this type of patient should be extremely low. In like manner, most deliveries are relatively simple, requiring but little obstetric manipulation, and therefore the amount of anesthesia required and the relaxation necessary should be minimal. And yet, one is confronted with the fact that anesthesia deaths contribute substantially to over-all maternal mortality.

The position that obstetric anesthesia holds, both in the field of obstetrics and in that of anesthesia, is frequently inferior. In many instances, the administration of the anesthetic is relegated by those who are in charge to the most inexperienced. The opinion seems to be, in a great many instances, that anyone—nurse, intern, resident, practicing physician, anyone that is handy—can competently give an obstetric anesthetic. As long as this type of thinking remains prevalent, the incidence of maternal deaths due to anesthesia will remain high.

In a review of the literature, of 4,894 maternal deaths, 182 (3.7 per cent) were caused by anesthesia.[1-26] This series represents a cross section of the United States. Hingson and Hellman[18] have reported a much larger series, gathered from the literature of both the United States and Europe, with a total of 330 anesthetic maternal deaths. The present report does not include theirs, although I am sure that many of the cases in this report are included in their statistics. Unfortunately, most of the published articles do not break down the anesthetic deaths as to the method of anesthesia, whether it was spinal, inhalation, caudal, local or intravenous. Therefore, it is difficult to ascertain which of the methods used was the most lethal. If only the reports in which the method of anesthesia was stated are considered there were 1,878 deaths, seventy-one of which were due to anesthesia. Of these, twenty-five were due to spinal anesthesia, thirty-nine to inhalation anesthesia, and seven to caudal anesthesia. The maternal mortality rates of Minnesota for 1941[9], 1950[17] and 1951[24] have been published. There were 237 maternal deaths reported in these three years. Of these, ten were due to anesthesia. This gives a proportion of 4.2 per cent, which is higher than that given for the total cross section of the country.

All methods of anesthesia have been used for obstetrics: inhalation anesthesia, conduction anesthesia and, in a small number of cases, intravenous anesthesia. All have been the cause for some deaths. Unfortunately, the vast majority of these deaths were preventable.

Inhalation Anesthesia

Various agents have been used in inhalation anesthesia, including nitrous oxide, ethylene, ether, cyclopropane, trichloroethylene and chloroform. All have their advantages as well as their disadvantages. The agent used should be the one with which the person administering the anesthetic is most familiar. Whenever inhalation anesthesia is used, there is always the problem of vomiting under anesthesia and aspiration of the vomitus. This has caused more deaths than any other factor. The solution of the problem appears to be to avoid giving this type of anesthetic if the mother has eaten within five to six hours before she comes to the delivery room. There appears to be no good reason why these women cannot be instructed by the obstetrician

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to stop taking food and drink when they feel they are going into labor. The reason given—that these gravid patients must eat to "keep up their strength"—is nonsensical and dangerous. Once an obstetric patient is in the hospital and is in active labor, there is never a good reason to feed her. Intravenously administered fluids can not only provide adequate fluid balance but also maintain the necessary caloric intake. Those patients who have come to delivery with a full stomach should under no circumstances receive an inhalation anesthetic. Other methods of anesthesia are available. Any of the conduction anesthetics can be used with safety if they are properly administered.

In regard to the administration of inhalation anesthetics, not everyone can give an inhalation anesthetic, not everyone can competently work a gas machine and even not everyone can "drop" ether competently. Only those persons who have been trained should be allowed to give an anesthetic. There is no argument who that person should be, whether nurse or physician, but at least he or she should have had training in the giving of the anesthetic. Often the inexperienced person will unwittingly allow the obstetric patient to become too deeply anesthetized, causing cardiac and respiratory failure. Frequently these inexperienced people will allow anoxia to be present and unrecognized, causing perhaps not death but severe brain damage not only to the mother, but also to the baby. Generally the inexperienced will be unable to cope with the patient who has vomited while under the influence of an anesthetic.

Conduction Anesthesia

Conduction anesthesia can be safe if it is properly managed. Among the forms of conduction anesthesia that are available to the obstetric patient are spinal, caudal and pudendal block. Spinal anesthesia is reported in the literature to be the second highest cause of maternal deaths due to anesthesia. Almost without exception, the death was due to too massive a dose of the spinal anesthetic agent.

For vaginal deliveries a minimal dose should always be given. Two and one-half milligrams of heavy solution of dibucaine hydrochloride (nupercaine hydrochloride), 2.5 to 3.5 mg. of weighted tetracaine hydrochloride (pontocaine hydrochloride), 30 to 35 mg. of piperocaine hydrochloride (metycaine hydrochloride) or 40 to 50 mg. of procaine hydrochloride will give adequate anesthesia for vaginal delivery. If larger doses are given, then only complications can be expected.

For cesarean section minimal doses again are an absolute necessity. My colleagues and I use only procaine or metycaine; 60 to 70 mg. of unweighted metycaine or 75 to 85 mg. of procaine will give adequate anesthesia for cesarean section. If a larger dose is used, the anesthesia will extend abnormally high, causing a drop in blood pressure and a sensory level that will indicate that the patient may have respiratory embarrassment due to depression and paralysis of the respiratory muscles.

The technique, as worked out by Adriani and his co-workers,[27,28] by which saddle anesthesia should be performed using a dextrose-weighted anesthetic agent, is a safe and proved method for the administration of this type of conduction anesthesia.

Caudal anesthesia, the use of which is largely due to Hingson and Edwards,[29,30] has proved also to be a safe method of conduction anesthesia, if the technique for the insertion of the needle and administration of the anesthetic agent is properly followed. There are certain inherent dangers and difficulties with caudal anesthesia. The greatest difficulty is the insertion of the caudal needle, which takes a great deal of practice. Caudal anesthesia should not be used unless the person administering it has received instruction from someone who has had experience in this method. The caudal technique can either be continuous, which means the giving of intermittent doses of the anesthetic agent as is necessary, or as a single dose for the expected short delivery. The danger of caudal anesthesia is the inadvertent placement of the caudal needle in the subarachnoid space, which results in giving the patient a massive spinal anesthetic. The height of the caudal anesthesia is so regulated that the level of anesthesia must extend at least to the sensory level of T10, the umbilicus, to insure that the patient will have pain-free contractions. If it extends higher than T6, uterine contractions will be completely stopped. For caudal anesthesia my colleagues and I have used 1.5 per cent solution of metycaine with good results. When the caudal needle is introduced, the patient is given a test dose of 5 to 8 cc. of the metycaine solution

and a time interval of at least five minutes is allowed to elapse in order to insure that the patient has not inadvertently received a spinal anesthetic. After this time lapse, the patient is given an additional dose of 20 to 30 cc., which, in the majority of cases, will produce adequate anesthesia with a sensory level between T10 and T11. The caudal anesthesia is then supplemented at regular intervals when the patient experiences pain. An additional dose of 10 to 15 cc. will, in most cases, give adequate relief.

Pudendal block is by far the safest of conduction anesthetic methods and is probably the safest of any of the anesthetic methods for a vaginal delivery. The pudendal nerve is blocked at Alcock's canal, which lies to the medial surface of the ischium in the region between the ischial spine and the tuberosity. This block, which is done bilaterally, plus infiltration of the labia majora up to the mons pubis, will give anesthesia to the lower part of the birth canal.[31] Although this block does not produce the marked relaxation that is found with saddle or low spinal and caudal anesthesia, it does have the advantage that, with a little practice, uncomplicated vaginal deliveries can be done with ease and the episiotomy and the repair can be done without pain to the patient. The most frequent complication of this block is inadvertent introduction of the needle into the rectum. This can be prevented by inserting the index finger of the opposite hand into the rectum and guiding the needle along the ischial tuberosity in the direction of the ischial spine. The second most frequently encountered complication is the intravascular injection of the anesthetic agent. Frequent aspirations on the barrel of the syringe will show whether or not the needle is in a blood vessel.

Cesarean Section

In our institution, the vast majority of cesarean sections are done with the patient under local anesthesia. Once the baby has been delivered, the patient is then given a general anesthetic in the form of intravenous pentothal sodium for the remainder of the procedure. The abdominal wall is thoroughly blocked, using a 0.5 per cent solution of metycaine. This means that the skin and the subcutaneous tissue down to the fascia are thoroughly infiltrated with the anesthetic solution. Most of the pain from a cesarean section appears to come from traction at the lower end of the incision. Therefore, we put a rather large amount of anesthetic agent into the suprapubic space of Retzius. Once the baby has been delivered and the cord has been clamped, the patient is given pentothal sodium for anesthesia during closure of the uterus, peritoneum and abdominal wall. My colleagues and I feel that it is absolutely necessary to instruct the patient that this is the safest possible way for the procedure to be done and, in most instances, the patient is more than willing to go along with our desires.

Prevention of Anesthetic Deaths

What are the things one can do in an attempt to eliminate the anesthetic factor in maternal mortality?

1. Personnel should be trained to administer the anesthetic. In surgery this fact is well recognized and accepted without question. Here one insists that the anesthesiologist or the nurse anesthetist administering the anesthetic must be trained to give adequate relaxation, that he must be able to cope with any emergency that arises during the course of the anesthesia and that he make sure there are no episodes of anoxia. It is just as important in obstetrics as in surgery that this type of person should be at the head of the table administering the anesthetic. Even if there is a shortage of personnel in the hospital, it is still reasonable that one or two people should be adequately trained to administer anesthesia properly.

2. It behooves the obstetrician to instruct his patients that when they are in labor they should not take food nor drink.[32] In this way inhalation anesthetics can be administered with safety. The old idea of trying to wash out the stomach by introducing a lavage tube is of no avail. The only possible good it can do is to induce vomiting by the patient and in this way rid the stomach of its contents.[33] In the hospital, as has been pointed out, there is never a good reason for feeding a patient in labor.

3. It must be remembered that the anesthetic death rate does not tell the entire story. It does not tell how many mothers were near death, nor does it tell how many accidents which were not fatal could have been prevented if good anesthetic management had been instituted. Unfortunately, these cases are never reported and only the fatal cases are drawn to our attention. These

cases of near death and of preventable accidents are just as important and should teach just as good a lesson as the fatal cases. If the obstetrician is convinced that inhalation anesthesia is the type of anesthesia that gives him the best results, then he must instruct his patients of the dangers of a recently eaten meal. On the other hand, if he feels that conduction anesthesia in any of its forms is the anesthetic of choice, then it behooves him to inform his patients of this, so that they will expect to receive conduction anesthesia. If the obstetrician feels that pudendal block is the safest method, and this fact is explained to the patient, making her fully cognizant that she will have some pain, the vast majority will be more than willing to acquiesce in the obstetrician's desire for a local anesthetic. These women are in a good position to bargain with. They realize that not only their own safety is at stake, but also that of the unborn child. Most of them will go to any extent to make sure that nothing unforeseen happens.

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Chronic Hypervitaminosis A

Report of a Probable Case in a Man

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VITAMIN A intoxication is probably a more common disease in the United States than its famous counterpart, vitamin A deficiency.[1,2] In Caffey's opinion routine administration of vitamin A to healthy, well-nourished infants and children constitutes a greater danger to their well-being than its omission.[3,4] In contrast to the wide dissemination of knowedge concerning vitamin A deficiency, the fact that vitamin A has definite toxic properties is frequently not appreciated. Modern texts on medicine and related sciences still emphasize hypovitaminosis A. The sections devoted to the opposite nutritional extreme, vitamin A intoxication, frequently fail to do justice to the importance of this disease in the everyday practice of medicine in this country;[5] some widely used treatises omit hypervitaminosis A entirely.[6] The widespread use of vitamin A preparations as supplements in infant feeding, which are often continued to school age, the massive doses which are on occasion employed for the treatment of some common skin disorders, (5f, 5g, 6c) "therapeutic trials" in conditions for which no specific remedy is known,[7,8] advertising claims and over-the-counter sales make chronic hypervitaminosis A a possible concern to the diagnostician. The true importance of the disease will remain unrecognized until its manifestations become more widely known.

Eskimos have realized, apparently since time immemorial, that the livers of polar bears, bearded seals, and arctic foxes are unfit for consumption by humans or dogs.[9] White men learned about these facts through the bitter experience of polar explorers. There is an account of acute vitamin A intoxication, which occurred on Novaya Zemlya on May 31, 1597: In an effort to find a North East Passage to India the citizens of Amsterdam had equipped an expedition under the command of William Barntzoon, "a most skillful mariner and burgher of Amsterdam." The expedition had reached Novaya Zemlya in August, 1596. There the members "were forced, in great cold, pouerty, misery and griefe, to stay all that winter" (*sic*) as reported by their historian, Gerrit de Veer. By spring the food situation had become desperate and the men took the liver of a bear which they had killed "and drest and eate it; the taste like us well, but it made us all sicke, specially three that were exceeding sicke, and we verily thought that we should have lost them all, for all their skins came of from the foote to the head; but yet they recouered againe, for the which we gave God heartie thankes, for if as then we had lost these three men, it was a hundred to one that we should neuer have gotten from thence, because we should haue had too few men to draw and lift at our neede" (*sic*).[10] Subsequent generations of arctic explorers have attested to the accuracy of Gerrit de Veer's description of polar bear liver poisoning.[11,12] Rodahl and Moore attribute the toxicity of polar bear and bearded seal livers to their high vitamin A content. Ingestion of one pound of these livers provides about 10,000,000 units of vitamin A; administration of 40,000 units vitamin A to a 250 gram rat is definitely poisonous.[13,14]

Polar bear liver poisoning is the prototype of the acute vitamin A intoxication which has been described following accidental ingestion of single large doses of vitamin A preparations or of large quantities of foods which have a high vitamin A content.[2] The abrupt onset of the illness, the gastrointestinal disturbances which accompany it, and the history greatly facilitate the diagnosis. In contrast, the manifestations of chronic vitamin A intoxication begin insidiously, gastrointestinal disturbances are absent, and patients frequently fail to volunteer information regarding their vitamin A intake unless they are questioned specifically. Symptoms referable to the central nervous system (headache, irritability, lethargy) and lesions of the integument are common to both acute and chronic hypervitaminosis A.

The author wishes to thank Dr. C. J. Watson and Dr. B. J. Kennedy for the opportunity to study this case.

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Although carotenoids are precursors of vitamin A in the human body, they will not cause any untoward reactions even if large amounts are ingested. Only vitamin A itself is toxic. Its precursors are apparently harmless. They are not converted into vitamin A in sufficient amounts to cause hypervitaminosis. To the contrary, carotenemia is likely to be associated with diseases which tend to cause endogenous vitamin A deficiency. It occurs in diabetes mellitus, hypothyroidism, Simmond's cachexia, male castrates, chronic glomerulonephritis, acute hepatic disease, and malnutrition. Lipemia, thyroid, and androgen deficiency seem to be involved in its pathogenesis. Carotenemia is characterized by a lemon to orange-yellow discoloration of the skin involving chiefly areas which have heavy stratum corneum (palms, soles, forehead, nose); the sclerae and mucous membranes remain unaffected. The discoloration is due to an excessive accumulation of cartenoids in the body and associated with a high plasma carotene level; the plasma vitamin A level remains normal. Skin pigmentation does not develop in healthy individuals even after ingestion of large amounts of carotene, and it is the only outward manifestation of carotinemia in those who are susceptible. The discoloration will disappear when the underlying disease abates.[15,16]

Chronic hypervitaminosis A, as it is seen in the United States today, was described and recognized in experimental animals thirty years ago: Takahashi, Nakamiya, Kawakami, and Kitasato fed excessive amounts of a crude vitamin A concentrate to mice and rats and found that their animals suffered loss of hair, emaciation, paralyses, and ultimately death; at autopsy fatty degeneration was found in the liver, heart, and kidneys, intestines and lungs were hyperemic and on occasion contained hemorrhages.[17] The possibility that these lesions might have been due to substances other than the vitamin A in their crude "Biosterin" was entertained for many years. But it is now established that vitamin A can produce lesions of the integument, gastrointestinal tract, and skeleton, as the Japanese workers had contended. These lesions are not due to fatty acids, vitamin D or other substances. They are not produced by fish liver oils in which vitamin A has been inactivated, but they can be evoked by administration of synthetic vitamin A acetate.[18,19,20,21] Rats and mice are not the only species susceptible to hypervitaminosis A; the disease has also been produced in guinea pigs, dogs, ducks, and chicks.[9,21] A hemorrhagic tendency, similar to that seen in scurvy, is prominent in many species. The adrenal cortex shows changes akin to those caused by vitamin C deficiency, especially in the guinea pig. But administration of vitamin C neither prevents nor counteracts hypervitaminosis A. Hypoprothrombinemia has been found in rats with vitamin A intoxication; however, it is not a constant feature of the disease and it does not respond regularly to vitamin K administration.[23,24]

Chronic hypervitaminosis A may produce skeletal lesions which are of diagnostic importance.[3,4,9,25] X-ray examination may reveal hyperostoses, mottling of the bones, thinning of the cortices, and decalcification. The roentgenograms may resemble those seen in infantile cortical hyperostosis, syphilis, low-grade infections, or healing fractures. In experimental animals excess vitamin A causes accelerated maturation and degeneration of epiphyseal cartilage, excessive remodeling of bone, increased osteoclastic activity leading to loss of cortical substance and multiple fractures; the fractures heal readily by voluminous callous formation. Hypervitaminosis A, like other metabolic disturbances, produces skeletal abnormalities most readily in young and growing individuals.

Iatrogenic hypervitaminosis A antedates the discovery of the vitamin.[16,17] Czerny, in 1912, reported development of seborrheic dermatitis in children with tuberculosis following administration of large doses of cod liver oil.[28] Nevertheless, Lehman and Rapaport, as late as 1940, maintained that vitamin A may be administered to children in doses of 300,000 units per day without any ill effects.[29] The first well-documented case of chronic hypervitaminosis A was reported by Josephs in 1944.[30] The patient was a three-year-old boy who had received daily 240,000 units of vitamin A in the form of halibut liver oil for almost his entire life. His height was normal, but he was underweight and anorexic. He had no eyebrows, and his hair was coarse, dry and brittle. Roentgenograms revealed thinning of the cortices on his phalanges and metacarpal bones; the proximal epiphyses of his humeri and tibiae were mottled, and skeletal development was advanced. When vitamin A medication was withheld, the patient showed rapid improvement; normal hair

growth resumed after two months, his appetite became normal, and he gained weight.

In the past ten years over twenty cases of chronic hypervitaminosis A have been reported in the pediatric literature in the United States.[2,3,4,30,31,32,33,34] The children were one to four years of age and had ingested at least 75,000 units vitamin A per day for a minimum of six months. The most conspicuous feature of the disease were bony, tender, subcutaneous tumors. Pain in the lower extremities prevented some of the patients from walking. Alopecia, rhagades, dry skin, hepatomegaly, and jaundice were common. The clinical picture suggested vitamin deficiency rather than vitamin intoxication, but the disease responded dramatically to the withdrawal of vitamin A medication. Bone pain subsided within days although the plasma vitamin A level required weeks to return to normal; the hyperostoses regressed only over a period of months. No permanent sequelae have been reported.

The relatively large doses of vitamin A required to cause hyperostoses in children may lead one to believe that vitamin A is rather innocuous after all, but hyperostoses develop quite late in the disease. They are undoubtedly preceded by months of malaise which may be difficult to evaluate in a young patient. A substance purported to be as beneficial as vitamin A is not likely to be thought of as the cause of a child's vague complaints.

Although the onset of chronic vitamin A intoxication should be easier to recognize in the more articulate older patient, the first well-documented case of chronic hypervitaminosis A in an adult was reported only three years ago.[35] Two more cases have been recorded since.[36,37] All of them occurred in women who had taken 100,000 to 600,000 units vitamin A daily. Initial symptoms appeared after about a year and included insomnia, irritability, malaise, headache, nausea, anorexia, weight loss, depression, diplopia, blurred vision, dysuria, urinary incontinence, arthritis, dysmenorrhea and hypomenorrhea. Loss of hair, including eye brows, eye lashes, pubic and axillary hair, desquamation of the skin and chloasma developed later. Exophthalmos, papilledema, nystagmus, unequal reflexes, positive toe signs and abnormal electroencephalograms have led physicians to mistake chronic vitamin A intoxication for brain tumor, meningitis and encephalitis. One of the patients had been on 500,000 units vitamin A per day for eight years; during this time she had undergone a craniotomy and developed some skeletal deformities and muscular atrophy. When chronic hypervitaminosis A was finally suspected and the fasting plasma vitamin A concentration determined it was found to be 2,000 microgram per cent.*

Despite occasional statements to the contrary, especially in the older literature, there can now be little doubt that excessive intake of vitamin A is toxic to man. Assessment of the optimal nutritional status of man with respect to vitamin A is beset with difficulties. The desirable vitamin A intake for an adult is variously estimated to lie between 2,000 and 7,000 units per day. In the United States, 5,000 units are recommended for normal adults, and it is believed that this dose should be increased to 6,000 units during pregnancy, and to 8,000 units during lactation; the recommended doses for children are 1,500 units to age one year, 2,000 units from age two to three years, 2,500 units at age four to six years, and 3,500 units at age seven to nine years.[38] One of the most careful studies concerning the vitamin A requirements of man was carried out in England during World War II on young adults.[39] One thousand three hundred units vitamin A per day were sufficient to maintain these individuals free of any signs of deficiency, and 2,500 units constituted a safe margin. Only three of eleven subjects who were placed on a vitamin A deficient diet developed night blindness. It began after they had been on the diet for seventeen to twenty-two months, and it was cured by administration of 1,300 units vitamin A per day; no massive doses of vitamin A were required.

Carotenoids are less effective in the prevention of hypovitaminosis A than vitamin A itself and their effectiveness depends in large measure on the form in which they are administered. Ingested as solutions in oil they seem to be quite readily utilized, but in form of carrots they are rather inactive. Diseases of the liver and possibly diseases of the intestine interfere with the conversion of carotenoids to vitamin A. Where absorption of fat is impeded, for instance in sprue and celiac disease, absorption of vitamin A and carotenoids is likely to be faulty, also. Patients with

*1 microgram vitamin A corresponds to 3.3 international or USP units vitamin A. The normal range of fasting serum or plasma vitamin A concentration is in the order of 20 to 60 microgram per cent.

diseases of this type may require an increased intake of vitamin A to forestall deficiency.

Understanding of the processes involved in the absorption and utilization of vitamin A and its precursors is still only fragmentary. Until more pertinent information along these lines becomes available, it will be impossible to determine the optimal nutritional status of man with respect to vitamin A with certainty. As far as the normal individual is concerned, there has been a tendency to overestimate the vitamin A requirements and to underestimate the dangers inherent in overdosage. The margin of safety between preventive and toxic doses may be appreciably smaller than is generally believed. Gerber, Raab, and Sobel[37] have observed symptoms indicative of chronic hypervitaminosis A in an adult who took as little as 50,000 units vitamin A per day for a period of eight months.

At the present time, the diagnosis of both vitamin A deficiency and intoxication must be made essentially on clinical grounds. Biophotometric measurements and determinations of the serum vitamin A concentration are of value only when they are interpreted in conjunction with the history and clinical findings. The cardinal manifestations of hypovitaminosis A are seen in the eye and the integument. They consist of follicular keratosis, nyctalopia, xerophthalmia, Bitot's spots and keratomalacia. The diagnosis should be made only if a reliable history of low vitamin A intake can be obtained, or if the patient suffers from a gastrointestinal, metabolic, or hepatic disease. The serum vitamin A level may be within normal limits if the patient has ingested vitamin A containing foods in the recent past.[41] On the other hand, a low fasting serum vitamin A level is not in itself diagnostic of vitamin A deficiency. The disease should respond to a normal vitamin A intake. Chronic hypervitaminosis A manifests itself chiefly by signs and symptoms referable to the central nervous system, the integument, and the skeleton. They may include headache, malaise, insomnia, irritability, nervousness, increased intracranial pressure, anorexia, weight loss, loss of hair, coarse hair, desquamation of the skin, hyperpigmentation of the skin, pruritus, joint and bone pain, skeletal deformities, hyperostoses, and decalcification. Roentgenograms are valuable adjuncts in the diagnosis when they do reveal skeletal abnormalities. A reliable history of high vitamin A intake is of paramount importance. The vitamin A level should be elevated before excess vitamin A medication is withdrawn, but it may return to normal before the last vestiges of the disease have disappeared. The patient should recover when given a normal diet without vitamin A supplement.

Probable Case in a Man

A fifty-four-year-old white interior decorator and real estate broker was admitted to the University of Minnesota Hospitals in May, 1954, with the chief complaint of pain in his left leg.

He had been in good health until nineteen months prior to his admission when he began to experience periodic episodes of indigestion. These episodes occurred usually in the afternoon, were not related to meals, and were relieved by belladonna, sodium bicarbonate, "cokes", or plain water. Seven months prior to his admission he consulted a physician for his symptoms of gastric distress. Physical and neurological examinations, roentgen studies of his gastrointestinal tract, and laboratory tests failed to reveal any abnormalities. The patient weighed 136½ pounds and there had been no weight loss. Symptomatic treatment resulted in some improvement.

During subsequent months the patient became mildly depressed. Two months before his admission he consulted the physician again because of severe neuritic pain in his left hip and leg. The pattern of pain corresponded to the distribution of the femoral nerve. The sedimentation rate was normal. Treatment with salicylates was instituted. A few days later weakness, headache, anorexia, and a low-grade fever developed. Physical examination was again negative, except for a decreased patellar reflex on the right; this abnormality persisted for only a few days. Roentgenographic examination of the chest and pelvis failed to reveal any disease process. The white cell count was 16,300 per cubic millimeter, with 22 per cent neutrophiles, 68 per cent lymphocytes, 5 per cent eosinophiles, and 5 per cent monocytes. The cephalin flocculation test was 3+. Other laboratory determinations, including urinalysis and bromsulfalein excretion, were within normal limits. Within one week the patient seemed to have largely recovered from his acute illness, except for some residual pain in his left thigh and a general feeling of malaise.

The patient was admitted to the University of Minnesota Hospitals (two months after the onset of his acute illness) for further diagnostic study. He related that he had had an attack of "arthritis" in his left hip "many years" previously and a moderately severe alcohol intake until about seven years prior to his admission. No history of exposure to heavy metals could be elicited. The patient thought that he might have had some undue exposure to solvent vapors in the months immediately preceding his acute illness. Questioned specifically concerning his vitamin A intake, the patient stated that he had had a mild eczema on his leg three years prior to admission. At that time his physician prescribed vitamin A by mouth in doses of 50,000 units per day. The eczema seemed to respond to this treatment, although it recurred on occasions on either leg,

especially during the winter months. The patient had continued to take vitamin A daily in doses of 50,000 units until the onset of his acute illness two months prior to admission when he stopped the medication on his own volition.

Physical examination revealed a well-developed, thin male in no acute distress. His temperature was 98.0°, pulse 72 per minute, respiration 18 per minute, blood pressure 120/70, weight 127 pounds. The tongue showed a mild tremor. The liver was palpable two fingerbreadths below the right costal margin. A small inguinal hernia was present on the right. The prostate was moderately enlarged (2+), symmetrical, non-tender, and of normal consistency. The left patellar reflex was absent; there was some weakness and atrophy of the quadriceps muscle and weakness of the tibialis anterior on the same side. Both ankle reflexes were diminished. No other abnormalities were found on physical or neurological examination.

A roentgenogram of the chest, an electrocardiogram, and urinalysis were within normal limits. The sedimentation velocity was 2, 6, and 9 mm. at 20, 40, and 60 minutes, respectively. The hemoglobin concentration was 15.2 gram per cent. The white cell count was 17,200 per cubic millimeter with 59 per cent neutrophiles, 28 per cent lymphocytes, 9 per cent monocytes, and 4 per cent eosinophiles. The stool gave a 4+ guaiac test on two occasions (on a diet containing meat). The bromsulfalein retention was 1 per cent, serum bilirubin 0.1 milligram per cent at 1 minute and 0.3 milligram per cent total. Cephalin flocculation was negative, thymol turbidity 3 units. The total lipids were 29 units. The prothrombin time was 13.2 seconds (control 13.1 seconds). The blood glucose concentration was 95 milligram per cent. The Mantoux test was positive at a dilution of 1:1000. The Kline test was negative. The erythrocyte protoporphyrin was 65 microgram per cent, the erythrocyte coproporphyrin 0.5 microgram per cent, the hematocrit 48 per cent. Urinary coproporphyrin excretion was 224 microgram in twenty-four hours. The Addis count (on a twelve-hour urine specimen consisting of 470 milliliters) was: casts 13,050, erythrocytes 1,720,000, leukocytes 11,750,000, negative for protein. A fasting serum vitamin A level was 69 microgram per cent with a carotene level of 228 microgram per cent (normal values for our laboratory are 20 to 40 microgram per cent for vitamin A and 120 to 200 microgram per cent for carotene).

The patient was placed on a regular diet. Since his discharge seven months ago he has continued to improve gradually without any further treatments.

Except for periodic outbreaks of eczema on his lower legs this fifty-four-year-old man was apparently in good health until eighteen months after he had begun to take 50,000 units of vitamin A daily. At that time ill-defined gastrointestinal symptoms developed which responded partly to non-specific measures. He became moderately depressed and finally contracted neuritic pain in his left hip and thigh and a mildly febrile illness with leukocytosis, eosinophilia, and a normal sedimentation rate. The outstanding findings on physical examination were hepatomegaly, an absent patellar reflex on the left, and atrophy of the quadriceps muscle. His hemoglobin concentration was normal, but there was some bleeding from the intestines. When vitamin A was discontinued he improved rapidly for one week and more slowly in subsequent months.

The essential signs and symptoms which this patient manifested have all been recorded in similar combinations in hypervitaminosis A. All three adults with chronic hypervitaminosis A described in the literature thus far had anorexia, weight loss, headache, malaise, depression, arthropathies, and neuropathies.[35,36,37] Gastrointestinal disturbances are prominent after ingestion of excessive amounts of vitamin A. Hepatomegaly is common in hypervitaminosis A in children; it has also been described in the adult.[37] Various alterations in liver function tests, usually minor and inconsistent, and fatty metamorphosis of the liver have been seen in this disease.[36,37] Hemorrhagic diatheses[36] and intestinal bleeding[17] may be features of this illness, as may leukocytosis,[35] eosinophilia,[36] febrile episodes,[37] and normal sedimentation rates.[37] Following withdrawal of vitamin A medication and on a normal diet, most of the patients reported on showed a brief period of rapid improvement, followed by a more gradual decline of signs and symptoms. Loss of hair, which was a conspicuous sign in the three other adults, was not prominent in our patient.

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Psychiatric Out-patient Treatment

A Questionnaire Survey

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IN A previous paper published in MINNESOTA MEDICINE, a report was made of a questionnaire survey of 342 patients who had received out-patient psychiatric treatment in one of the state-supported mental health centers.[1] Since this report was published, 500 additional patients have been referred to the Southern Minnesota Mental Health Center* for diagnosis and/or treatment.

As stated in the previous article, this state-supported out-patient center has a three-fold purpose: (1) to provide follow-up care for patients provisionally discharged from state mental institutions, (2) to provide treatment for psychiatrically indigent residents of Minnesota upon referral by a licensed medical doctor, and (3) to act as educational centers in applications of mental health.

The staff consists of a part-time psychiatrist serving as medical director, a clinical psychologist, a social worker and a receptionist-stenographer. Treatment consists primarily of eclectic psychotherapy in which reassurance, interpretation and re-education play a major role. The clinical team participates in treatment under the direction of the psychiatrist.

As a result of improved statistical accounting procedures of the Department of Public Welfare, valuable data was collected on the 234 new patients accepted for treatment during the 1953-54 fiscal year. In the opinion of the staff, an opportune time existed for an evaluation of the reactions of these new patients to treatment received. It was felt that patient attitudes, plus the statistical data on such variables as their age and sex, number of therapeutic contacts, psychiatric diagnoses, prior treatment and source of referral might provide a more complete appraisal of the services rendered by the Albert Lea installation.

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*Formerly the Community Mental Health Center.

Statistical Characteristics of the Patient Population

The population included in this study are the 234 new patients referred for services from the period July 1, 1953 to June 30, 1954.

Age.—The 234 patients ranged in age from three years to eighty-three years. The median chronological age was 18.9 years.

Sex.—Fifty and nine-tenths per cent of new admissions were males while 49.1 per cent were females. In the child population (eighteen years and under) about twice as many boys as girls were referred. Among the adults, the proportions were reversed.

Source of Referral.—Table I contains the primary sources of referral, i.e., the persons or agencies who originally suggested that the patient seek psychiatric help.

TABLE I

Referral Source	No. of Children (Under 18)	No. of Adults (Over 18)	Percentage of Total Case-Load
State hospital staffs	0	10	4.3%
Self, family, friends, relatives or employer	7	5	5.2%
Public welfare agencies	25	3	11.9%
Private welfare agencies	1	0	.5%
Licensed physicians	46	114	68.3%
Courts	1	0	.5%
Schools	16	0	6.9%
Ministers	1	1	.7%
Others	1	3	1.7%
Total	98	136	100. %

With the exception of patients referred directly by licensed physicians, all patients were required to obtain a medical examination prior to admittance to the center.

Prior Treatment.—Of the 234 new patients, 81.6% had received no prior treatment or psychiatric consultation of any sort. A total of 7.7%

of the population had been hospitalized in a state mental hospital prior to admission. Only 6.5%, or fourteen patients, had received prior psychiatric treatment on a private basis. Six of the fourteen were referred by the private psychiatrist because of the inability of the patient to pay for private care. The remaining 4.2% had received prior help from such sources as traveling psychologists from the Department of Public Welfare, the University Hospital and VA out-patient clinics.

Number of Therapy Contacts Per Patient.—An average of 8.3 treatment contacts were recorded for each adult patient and an average of 4.4 treatment contacts per child patient were made.

Psychiatric Diagnoses of Patients Seen.—The largest percentage of patients were diagnosed as suffering from some form of psychoneurosis (35. 3 per cent). About 5 per cent of the cases were diagnosed as having a psychosis upon admission. Learning difficulty and/or mental deficiency were the diagnoses applied to 17.4 per cent of the cases. Transient situational personality disorders comprised 11.9 per cent of the cases. Behavior disorders and character disorders comprised 7.8 per cent of the case load. The remaining 22.6 per cent were distributed among trait disturbances, special symptom reactions, and chronic brain disorders.

Results of Questionnaire Survey

In order to evaluate the reactions of the new patients to treatment, an eight-item questionnaire was devised and mailed to the 234 patients included in this study. In the directions for completing the questionnaire, the patient was encouraged to indicate freely his personal reaction to the questions. The directions further emphasized that if the patient so desired, the questionnaire could be completed with his or her name omitted.

Of the 234 questionnaires mailed, fourteen were returned because of improper addresses, leaving a total of 220 questionnaires which were presumably received by the patients or guardians of patients. From the total of 220 mailed questionnaires, 112 returns were received by the time of our self-imposed cut off date, one month later. This yielded a 51.4 per cent return. Many questionnaires were returned blank with a note that their child was seen only for testing, not "treatment."

Not all the respondents answered each question. Each question is, therefore, treated separately in compiling the results.

Question I	No. of Responses	Percentage of Responses
I visited the Mental Health Center:	110	100.0
A. Only once	21	19.1
B. Less than 5 times	30	27.3
C. Between 5 and 10 times	28	25.4
D. Between 10 and 20 times	20	18.2
E. I am continuing to visit the Center	11	10.0

Question II	No. of Responses	Percentage of Responses
As a result of my visits to the Center, I feel:	97	100.0
A. Greatly improved	24	24.8
B. Much improved	49	50.5
C. Only slightly improved	14	14.4
D. That no improvement was made	10	10.3
E. That my condition is worse	0	00.0

Question III	No. of Responses	Percentage of Responses
I feel that coming to the Center:	97	100.0
A. Has upset me greatly	0	0.0
B. Made me more uncomfortable	5	5.2
C. Reduced some of the fears I had previously	31	31.9
D. Helped me in solving some of my problems	47	48.5
E. Actually prevented further mental or nervous difficulties	14	14.4

Question IV	No. of Responses	Percentage of Responses
In terms of help received, I feel I was (or am):	100	100.0
A. Aided greatly	25	25.0
B. Helped considerably	54	54.0
C. Helped some, but wanted more aid	18	18.0
D. Wasting my time	1	1.0
E. Actually harmed by visits	2	2.0

Question V	No. of Responses	Percentage of Responses
If any of my friends or relatives needed psychiatric help, I would:	105	100.0
A. Highly recommend the Center in Albert Lea	68	64.8
B. Suggest the Center as a possible place where help could be received	26	24.7
C. Mention the Center to them	11	10.5
D. Tell them of the Center, but only as a last resort	0	0.0
E. Tell them to seek help elsewhere	0	0.0

Question VI	No. of Responses	Percentage of Responses
For the treatment received, I would:	101	100.0
A. Resent having to pay any fee	1	1.0
B. Would pay a minimum fee if required	40	39.6
C. Would pay a reasonable fee if required	53	52.5
D. Would feel better if I could pay for services received	6	5.9
E. Feel that all patients should pay for treatment	1	1.0

Question VII	No. of Responses	Percentage of Responses
In the future, if I felt I needed further psychiatric treatment, I would:	84	100.0
A. Certainly not come back to the Albert Lea Center	0	0.0
B. Maybe go back to the Center, but only as last resort	4	4.8
C. Go back to the Center, but prefer to have private care	4	4.8
D. Come back willingly	40	47.6
E. Be eager to return because of help received in the past	36	42.8

Question VIII	No. of Responses	Percentage of Responses
Since my last contact with the center:	78	100.0
A. I was hospitalized for my condition	3	3.8
B. I have sought further psychiatric help	4	5.2
C. I have obtained help from others such as doctors, ministers, welfare workers, etc.	14	17.9
D. I am troubled only occasionally by my condition	36	46.2
E. I am feeling well and healthy	21	26.9

The last two questions were to be answered only by patients who had no further scheduled appointments with any staff member of the Center.

Conclusions

The 234 patients referred to the Southern Minnesota Mental Health Center during a twelve-month period were statistically studied and found to have a median age of 18.9 years. The case load was equally divided between male and female patients. Eight of ten patients referred had never received prior psychiatric help. About 68 per cent of these patients were referred directly by physicians of the community. About eight treatment contacts were made with each adult patient, while about four and one-half treatment contacts were made with each child patient. As for psychiatric diagnoses, the largest percentage of the case load falls in the psychoneurotic category with only 5 per cent diagnosed as psychotic.

An eight-item questionnaire was devised and mailed to the 234 patients in an effort to determine their reaction to treatment. In the directions for the questionnaires, provisions were made for patient anonymity. Of the 220 questionnaires presumed to have been received, 112 or 51.4 per cent were returned by our self-imposed cut off date.

The following conclusions appear warranted:

1. 75 to 79 per cent of the respondents indicated their condition as much improved or greatly improved. An additional 14 to 18 per cent indicated slight improvement (Questions II and IV).

2. 31 per cent indicated that some of their fears have been reduced while 48 per cent felt they have received help in solving some of their problems (Question III).

3. 14 per cent of the respondents felt that further mental or nervous difficulties have actually been prevented (Question III).

4. 65 per cent would highly recommend the Center to friends or relatives, while none of the respondents indicated that they would disparage the Center (Question V).

5. As for payment of fees for treatment received, 92 per cent indicated that they would pay

(Continued on Page 650)

Hypertensive Encephalopathy versus Schizophrenia

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THIS case history is presented as an example of how an organic illness, hypertensive encephalopathy, was mistakenly diagnosed schizophrenia.

A man, aged fifty-six, was referred to the Anoka State Hospital on December 14, 1954, as a severely disturbed schizophrenic patient. For the four days before admission, he had been hospitalized elsewhere because of his destructive behavior. He required restraints and presented such a severe problem that the management insisted he be transferred to the state hospital.

On admission, the patient was ambulatory, did not appear acutely ill and gave the following history of the presenting illness. "I went to the neighbors about a week ago and they asked me to stay with them for a few days and I went to bed, awakened, and they told me my closest friend had just died. I was upset because he was my best friend, but I went completely to pieces when he walked in the door and returned from the dead. Then there was a lot of excitement and a lot of people were running in and out, and there were a lot of automobiles and strange lights."

He remembered being examined by a doctor and of going to a local hospital. After arriving there, he felt that others talked about him and threatened him. He went on to say, "They told me that if I married one of the nurses, my life would be spared. I refused and they shot at me and I ran away from them and they chased me through fields and over church steeples. They finally captured me and took me back and put me in a cage." He felt that he needed to come to Anoka State Hospital, as he had gone through so much that he was close to a nervous breakdown.

He gave a scrambled version of his past history with an involved story about different insurance examinations and various doctors who had treated him. Nevertheless, he had been in comparatively good health and able to do farm work with supplementary labor on the highway until a few months before the present illness. He had some discomfort in the back of his head and neck, pains in his chest, had trouble with his vision and some loss of memory. He had been taking medicine for several weeks for high blood pressure and kidney trouble. During the initial examination the patient's level of awareness fluctuated. At times, he seemed in good contact, talked coherently and evidenced good motor control. Then, again, he was confused, disorganized, incoherent and inco-ordinated.

He was seen by our consultant in internal medicine who noted the following: Blood pressure was 200/140. The heart was enlarged, with A-2 about three times as loud as P-2. There was a Grade III retinal arteriosclerosis with hard white spots (edema residues), with marked narrowing of lumen of arterioles to ⅓ or ¼ the lumen of the retinal veins. A slight choked disc and a few white spots which looked like cotton wool exudates were noted. The examination of the retina of this patient gave a clue to the probable cause of his symptoms. The arteriolar lumen of all of his retinal arteries was from ½ to ⅓ the normal diameter. Poiseuille's Law states that the quantity of fluid flowing through a vessel under a given head of pressure is proportional to the 4th power of the diameter. Therefore, if the diameter of a tube is reduced ½ only 1/16 of the previous volume flow is present. The retinal arterioles are part of the brain arterial system, and if the same condition of spasm would exist in the arterioles of the brain or even one part of the brain, the blood supply to this part of the brain would be enormously reduced. In consequence, there would be an inadequate supply of blood sugar, oxygen and other substances necessary for normal metabolism. Products of normal as well as abnormal metabolism would pile up, causing altered cerebral function. The exudates of the retina, as well as hemorrhages of the retina, would probably be reproduced in these inadequately nourished portions of the brain. The urine concentrated to a specific gravity of 1020, and there was some renal insufficiency, with blood-urea-nitrogen of 28 mg. per cent."

A diagnosis of hypertensive encephalopathy was made, and the patient was started on Serpasil orally. As his blood pressure decreased, he evidenced continuous improvement in his mental status. He remained cooperative with no disturbed behavior, and reassurance was given freely to help overcome the relatively mild confusion, delusions and illusions which presented at intervals the first two weeks of hospitalization.

After three weeks of hospitalization, the patient was discharged symptom-free, on a maintenance dose of Serpasil and a protein limit of 50 grams daily.

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Minneapolis Surgical Society

PREOPERATIVE USE OF A COMBINATION OF LEVO-DROMORAN TARTRATE AND A NEW NARCOTIC ANTAGONIST

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Fromherz and Pellmont[1] suggested, on the basis of experiments in animals, that the respiratory depression produced by Levo-Dromoran® Tartrate could be overcome by doses of a new narcotic antagonist, levallorphan tartrate,* which are smaller than those which inhibit analgesia. This leads to the interesting supposition that a ratio of these two morphinan derivatives might be found which, when given to man, would provide good analgesia without hazard of respiratory depression. The pharmacology of these drugs was investigated further by Benson et al.[2] Gross and Hamilton[3] were the first to study these agents in normal human volunteers. Utilizing the Wolff-Hardy-Goodell technique they found that, on simultaneous and subcutaneous administration, less levallorphan tartrate was required to prevent respiratory depression than was necessary to affect the analgesia produced by Levo-Dromoran Tartrate. Interestingly, when the drugs were given simultaneously by the intravenous route, there was respiratory depression in four subjects. Hamilton and Cullen were the first to report on the use of levallorphan tartrate in opiate-induced respiratory depression in man[4] and on its merits as a supplement to nitrous oxide-oxygen anesthesia.[5] Cullen and Santos[6] used a combination of the drugs (10 parts Levo-Dromoran Tartrate and 1 part levallorphan tartrate) in patients with chronic pain. This 10:1 ratio provided good analgesia without respiratory depression when given either subcutaneously or intravenously. In view of these findings, the present study was undertaken to determine the characteristics of the 10:1 mixture as a preoperative medication in comparison with morphine.

Procedure

The patients in this study were divided into two groups so that concurrent data with morphine could be obtained to serve as a standard for comparison. Ninety-eight patients received morphine sulfate subcutaneously as preoperative medication. Three hundred and sixty-four were given a premixed solution containing 5 mg. Levo-Dromoran Tartrate and 0.5 mg. levallorphan tartrate per cc. also subcutaneously.† For the sake of brevity, this mixture will be referred to in the text as "combined drugs" and the doses given expressed as mg. of Levo-Dromoran Tartrate. Special individual protocol forms were prepared so that all data relating to the pre and postoperative periods could be recorded.

The routine preoperative procedure was as follows: All adults, except those over sixty years of age or those for whom there was a specific contraindication, received 1½ grains of Nembutal® the evening before surgery. This dose was repeated in one hour if the patient was not resting comfortably. One and one-half grains of Seconal® were given 90 minutes preoperatively. Scopolamine (preserved with mannitol) or atropine and the narcotic were given subcutaneously forty-five minutes preoperatively. The dosage schedule for these drugs is shown in Table I.

TABLE I. PREOPERATIVE DOSAGE SCHEDULE

Age (Years)	Atropine (mg)	Scopolamine (mg)	Morphine (mg)	Combined Drugs (mg 1-Dromoran)
Under 1	0	0	0	0
1- 3	0.2	0	0	0
3- 6	0.3	0	0	1.0
6-10	0.3	0	*	1.5
10-12	0	0.2	8.0	2.0
12-60	0	0.3	10.0	2.5
Over 60	0.3	0	*	2.0

*Morphine given intravenously in operating room, p. r. n.

The dosage schedule of the combined drugs was arbitrarily chosen on the basis of our earlier experience with Levo-Dromoran Tartrate in the recovery room.[7] It will be noted that patients under ten or over sixty years of age did not receive morphine preoperatively in this study. In contrast, of those who were given the combined drugs, 4 per cent were under six and 11 per cent were seventy years of age or older. The oldest patient on the combined drugs was ninety-four. The poorer clinical status of those who received the combined drugs is shown by the following facts: In the morphine group 97 per cent were considered good and 3 per cent fair operative risks. On the other hand, only 83 per cent of the combined drug group were classified as good, 13 per cent as fair and 4 per cent as poor risk cases. Again, 4 per cent of the patients in the morphine group, as against 9 per cent in the combined drug group, had diseases other than those which required surgical intervention. We were not concerned over these disparities in the groups because we were of the opinion that if the combined drugs had significant advantages over morphine, they would become apparent in spite of the poorer clinical condition of the test group.

When the patients were brought to surgery, notes

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*Levallorphan tartrate is the generic designation for levo-3-hydroxy-N-allylmorphinan tartrate (RO 1-7700).

†The premixed solution of Levo-Dromoran Tartrate and RO 1-7700 was made available for this study in 10 cc multiple dose vials by Dr. M. J. Schiffrin, Hoffmann-La Roche, Inc.

TABLE II. PREOPERATIVE AND POSTOPERATIVE CONDITION

	Morphine	Combined Drugs
Total Number of Cases	98	364
Preoperative reactions		
Drowsy	56%	71 %
Sleep	8%	19 %
Nausea	2%	0.6%
Emesis	0	0.6%
Respiratory depression	11%	2 %
Hypotension	0	2 %
Hypertension	2%	0.6%
Bradycardia	2%	2 %
Tachycardia	1%	3 %
Euphoria	4%	7 %
Apprehension	9%	4 %
Vertigo	0	1 %
Others	0	0.3%
Reactions during surgery	3%	2 %*
Condition in recovery room		
Good	94%	96 %
Fair	6%	3 %
Poor	0	0.3%
Awake	52%	54 %
Drowsy	45%	45 %
Depressed	3%	0.3%
Total recovery room reactions	28%	9 %
Time in recovery room		
90 minutes or less	60%	69 %
91-120 minutes	17%	15 %
More than 120 minutes	23%	16 %

*Including death of cardiac arrest during surgery on the heart.

were made of their condition with particular attention being given to such reactions as: drowsiness, sleep, nausea, emesis, respiratory depression, hypotension, hypertension, bradycardia, tachycardia, euphoria, apprehension and vertigo. All inhalation anesthesia was given with assisted or controlled ventilation. Careful records were kept of reactions during surgery as well as of the amounts of other agents used during the operative procedures. Similarly, notes were made of reactions in the recovery room and of the length of time the patient remained there. Our standard procedure to keep patients in the recovery room for at least one hour, regardless of their condition, was followed in this study.

Results

An analysis of the results obtained is shown in Table II. The immediate preoperative condition of the two groups did not differ appreciably with reference to the incidence of nausea, emesis, hypotension, hypertension, bradycardia, tachycardia and vertigo. The combined drugs produced more sedation (90 per cent vs. 64 per cent) and euphoria (7 per cent vs. 4 per cent) than did morphine. The combination yielded less respiratory depression (2 per cent vs. 11 per cent) and less apprehension (4 per cent vs. 9 per cent) than did morphine. The anesthetists, who did not know which drug the patient had received preoperatively, could pick out those who were given the combined drugs because they were more relaxed and had better skin analgesia than the morphine group. There was no significant difference in the incidence of reactions during surgery (2 per cent for the combined drugs, 3 per cent for morphine). The only death in the two groups was a poor risk cardiac patient who had received the combined drugs and died of cardiac arrest during surgery on the heart.

There was no significant difference in the percentage of patients who were in good condition on admittance to the recovery room. It was significant, however, that in spite of the poorer preoperative clinical condition

TABLE III. REACTIONS IN RECOVERY ROOM

Reaction	Morphine (Per Cent of Cases)	Combined Drugs (Per Cent of Cases)
Cardiovascular	13%	5.0%
Respiratory Depression	5%	0.3%
Euphoria	2%	0.4%
Nausea or Emesis	2%	2.0%
Disorientation	2%	0.3%
Miscellaneous	4%	1.0%
Total	28%	9%

of those cases which were given the combined drugs, the incidence of depressed patients was ten times as great in the morphine group as in the combined drug group (3 per cent vs. 0.3 per cent). Moreover, there was a significant difference in the frequency of reactions in the recovery room; as can be seen from Table III, listing these reactions, their over-all incidence in the morphine group was 28 per cent, as contrasted by an incidence of 9 per cent in the combined drug group.

This difference in the frequency of reactions in the recovery room is paralleled by the difference in the time the patients of the two groups had to be kept in the recovery room. As appears from Table II, a higher percentage of patients in the combined drug group had a significantly shorter stay in the recovery room. This is all the more remarkable since these were the cases whose preoperative condition was generally poorer.

An analysis of the frequency with which various agents were used during surgery indicates a similar distribution in both groups. The frequency distribution in the combined drug group was as follows: Pentothal® was given in 325 cases; nitrous oxide and oxygen in 271; curare in 263; cyclopropane in 95; intrathecal Pontocaine®-ephedrine-dextrose in 71; Tensilon® in 35; ethyl ether in 19; combined drugs (intravenously) in 17; morphine (intravenously) in 15. Other agents used on five occasions or less were: Wyamine,® vinethene, atropine, cortisone, cocaine, insulin, Cedilanid,® procaine, and aminophylline. The average amount of Pentothal per patient in the morphine group was 682 mg. and in the combined drug group, 631 mg. Of the patients who in the combined drug group received Pentothal, 42 per cent required less than 500 mg., whereas only 32 per cent of the morphine group were in this category.

The advantages of the combined drugs were most apparent in poor risk patients, particularly in those in whom major surgery was performed. The following cases may serve as examples: A seventy-four-year-old woman, a very poor operative risk with a vital capacity of 1.2 liters, was given preoperatively 1.5 mg. Levo-Dromoran Tartrate (in combination with 0.15 mg. levallorphan tartrate) and 0.3 mg. atropine. She was relaxed but not sedated and had no preoperative reactions. An exploration of the right chest was performed using 750 mg. Pentothal, 21 mg. curare and endotracheal nitrous oxide-oxygen. Respirations were controlled throughout the procedure. There were no reactions during surgery, and she was awake and responding when admitted to the recovery room. All vital signs were stable. She was given 1 mg. Levo-Dromoran Tartrate (in combination with 0.1 mg. levallorphan tartrate) for pain relief and was released from

the recovery room after sixty minutes. The second example is that of an eighty-seven-year-old woman who had a cerebral accident with hemiplegia (four days' duration), a mediastinal tumor and who had swallowed an open safety pin. In spite of her very poor condition, 1.5 mg. of Levo-Dromoran Tartrate (with 0.15 mg. levallorphan tartrate) and 0.3 mg. atropine were given preoperatively. She was drowsy on arrival in surgery. An esophagoscopy was performed under Pentothal and curare, supplemented with endotracheal nitrous oxide-oxygen. Ten mg. Tensilon were given by the intravenous route immediately after completion of surgery. She was awake and comfortable when admitted to the recovery room. All vital signs were stable. She was returned to her room in sixty minutes. The oldest patient who received the combined drugs was ninety-four years of age. She had an uneventful and successful repair of a fractured hip using intrathecal Pontocaine-ephedrine-dextrose. The preoperative disorientation disappeared following the administration of 1.5 mg. Levo-Dromoran Tartrate (with 0.15 mg. levallorphan tartrate) and 0.2 mg. atropine.

Discussion

Our experience with the combined drugs indicates that they are safe, effective, predictable and have advantages over morphine as preoperative medication. There was with this combination better sedation and greater freedom from apprehension than with morphine. This is particularly advantageous in children. The combined drugs produced less respiratory depression preoperatively and postoperatively than did morphine. Pain and local reactions at the injection site were absent when the combined drugs were given. Occasional reactions of this type were seen after the administration of morphine sulfate.

The combined drugs provided for easier management of the patients during surgery. Intrathecal injections were more easily made. Pentothal and intravenous opiate requirements were reduced.

The wide variety of agents used during surgical procedures following the administration of the combined drugs attests to the safety of this new type of preoperative medication. In seventeen instances the combination was given intravenously as a supplement to nitrous oxide-oxygen anesthesia. The results were uniformly satisfactory.

The postoperative course of those patients who had received the combined drugs was better than that of those who had been given morphine. The former were more co-operative, better oriented, free of pain and easier to manage in the recovery room. The opiate requirements and the number of reactions in the recovery room were reduced in the patients who had received the combined drugs. Children were more sedated and easier to manage. The secondary effect on the parents was of no little consideration. Elderly patients did not "climb the walls," indeed, they were more mentally alert at times following the administration of the combination than they were beforehand. The over-all shortening of time in the recovery room was an important factor economically. The addition of 1 part levallorphan tartrate to 10 parts Levo-Dromoran Tartrate made it possible to provide intense analgesia without depression. Our experience has been so rewarding that the combined drugs have been made standard preoperative medication in this hospital.

Summary

1. A premixed combination of 10 parts Levo-Dromoran Tartrate and 1 part levallorphan tartrate was given preoperatively by the subcutaneous route without adverse effects to 364 patients. The results were compared with the effects of morphine in ninety-eight patients.

2. The combined drugs provided greater sedation, euphoria and freedom from undesirable reactions than did morphine. There was less apprehension and respiratory depression both pre and postoperatively when the combined drugs were used.

3. The amount of Pentothal and intravenous opiates required during surgery was reduced following administration of the combined drugs. The use of the combination preoperatively was compatible with a wide variety of agents commonly employed during surgical procedures.

4. Patients who received the combined drugs had fewer reactions in the recovery room and were sent back to the floor sooner than those who were given morphine.

Acknowledgment

The excellence and completeness of the individual records could not have been possible without the wholehearted interest and co-operation shown by the nursing staff on the floors and in the Department of Anesthesia. My sincere thanks to them all.

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Addendum

Since the establishment of routine use of the combined drugs, further experience has shown that scopolamine with the combined drugs can be given up to age seventy without danger of depression. No Seconal is given preoperatively to these patients.

When this paper was written, we did few tonsillectomies because of the polio season. Since then, the combined drugs have been used routinely preoperatively for tonsillectomy in children.

Our staff in the recovery room has reported that these children respond more quickly, have little or no nausea, require airways for a shorter time and need much less postoperative sedation than previously. As a consequence, the minimum time in the recovery room, post-tonsillectomy, has been reduced from sixty to thirty minutes.

Current Concepts

THE VALUE OF THE ELECTROCARDIOGRAM IN DIAGNOSIS

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Nearly fifty years have passed since Einthoven developed the electrocardiograph, and a quarter of a century since it became generally available. Today, thanks to the development of small, lightweight instruments, an electrocardiogram is regarded as a routine laboratory request in most general medical examinations and a requirement in any cardiac evaluation.

In the diagnosis of myocardial infarction, the usefulness of the electrocardiogram has been greatly extended by a more thorough precordial study using Wilson's unipolar leads. The six positions, V-1 through V-6, are generally agreed upon as necessary, with back leads or leads in higher or lower interspace levels desirable in certain doubtful cases. Smaller areas of infarction are now being detected with these leads. As a result, the over-all prognosis of myocardial infarction has doubled in the last fifteen years.

Coronary insufficiency remains a problem in diagnosis. An electrocardiogram taken at rest may be normal in the presence of definite coronary sclerosis. Various tests such as Master's two-step exercise test, are useful in detecting coronary insufficiency, but false negative, and, occasionally, false positive tests add to the problem.

Increased accuracy in the diagnosis of ventricular hypertrophy has followed more complete precordial lead studies. Many difficulties remain, however, especially when right and left ventricular hypertrophy are both present. The thoracic roentgenogram may reveal cardiac enlargement undetected by electrocardiography, and vice versa. A left ventricular strain pattern may appear before x-ray evidence of enlargement of the left ventricle in the early stages of hypertensive heart disease, and occasionally concentric left ventricular hypertrophy in aortic stenosis is more evident by electrocardiography than on fluoroscopy.

Arrhythmias remain the special province of electrocardiography. Here, the precordial lead V-1, overlying the right atrium, is especially useful. More or less continuous tracings are advisable in the conversion of ventricular tachycardia to normal sinus rhythm when intravenous Procaine amide is employed, allowing for better control and early recognition of toxic signs.

The rapid growth of cardiac surgery in congenital and acquired heart disease has called upon electrocardiography as an aid in correct presurgical diagnosis. For example, the presence of right axis deviation should raise immediate doubt as to the presence of uncomplicated patent ductus arteriosus. Similarly, left axis shift and evidence of left ventricular strain may point to significant mitral regurgitation in a case of mitral stenosis being considered for mitral commissurotomy.

Thanks to much electrocardiographic and pathologic investigation, the diagnosis of myocarditis is again fashionable, and myocardial involvement in the course of many types of viral disease and a host of other bacterial diseases, including pneumonia, diphtheria, and rheumatic fever, is recognized. Isolated, or Fiedler's, myocarditis is a particularly fatal form of unknown etiology. Myocardial involvement in the collagen diseases—lupus erythematosis, panarteritis nodosum, and scleroderma—may also be demonstrated by electrocardiography.

In differentiating primary idiopathic pericarditis, by no means a rare disorder, from acute myocardial infarction, the electrocardiogram is most valuable. The benign character of the former and the grave prognosis of the latter demand a correct differential diagnosis.

The electrocardiogram may also be useful in the diagnosis of a number of other diseases, including myxedema, thyrotoxicosis, beri beri, acute and chronic cor pulmonale, primary or metastatic tumors of the heart. It may also reveal effects of quinidine, digitalis, and electrolyte imbalance associated with hypokalemia and hyperkalemia and hypocalcemia.

The limitations of the electrocardiogram in diagnosis, unfortunately, are not generally recognized. Only a few of the patterns mentioned above are truly diagnostic. Left ventricular strain and coronary insufficiency are often impossible to differentiate, and both may be confused with digitalis effect. Beri beri, pericardial effusion, and myxedema may produce similar patterns. Even myocardial infarction is not necessarily a specific pattern, a similar one being produced by stab wounds of the heart. The boundary between normal and abnormal electrocardiograms may also be obscure and open to varying diagnoses by different electrocardiographers. The following current classification of electrocardiograms reflects these difficulties: within normal limits; probably normal; borderline ECG; probably abnormal; definitely abnormal ECG.

Finally, let us not forget that an electrocardiogram cannot be substituted for a well-taken history and a thorough physical examination.

Laboratory Aids

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George G. Stilwell, Editor

LABORATORY AID IN THE DIAGNOSIS OF LUPUS ERYTHEMATOSUS

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Systemic lupus erythematosus (LE) is a disease of unknown cause. Aggravating factors are recognized, such as infection, exposure to sunlight or cold, allergic reactions and surgical procedures. The general symptoms occurring during activity of the disease are fever, weakness, fatigue, prostration and loss of weight. Arthralgias and joint symptoms are seen in many patients, and often it is difficult, without prolonged follow-up, to distinguish between systemic LE and rheumatoid arthritis. Various cutaneous manifestations have been described, among them the classic open "butterfly wings" on the face. Evidence of disturbances of the central nervous system or of lesions of the pulmonary and cardiovascular systems occurs frequently. Lymphadenopathy and splenomegaly occur in more than 50 per cent of patients.

It has been stated that LE has assumed an importance disproportionate to its incidence as a clinical problem. The main factors responsible for this emphasis are (1) recognition of multiple systemic manifestations in LE in addition to cutaneous lesions, (2) development of technical procedures and criteria for more exact diagnosis, (3) increased interest in the entire group of so-called collagen diseases and (4) discovery of cortisone and corticotropin (ACTH), which offer a limited approach to treatment.

Laboratory findings include anemia, leukopenia, proteinuria and hematuria. Elevation of the erythrocytic sedimentation rate is frequently observed and is roughly proportionate to the activity of the disease. False positive results of serologic tests for syphilis may occur.

The LE Cell

In 1948, Hargraves and associates described a peculiar cell in the buffy layer of bone marrow taken from patients who had acute and subacute lupus erythematosus. This cell, the well-known LE cell, is a mature polymorphonuclear leukocyte containing an ingested or lysed mass of homogeneous, pale-purple material thought to be of nuclear origin. It was noted also that several polymorphonuclear leukocytes might be attracted to a single large mass of lysed nuclear material, forming a "rosette." A cell similar to but not identical with the LE cell was described in the bone marrow of patients who had a variety of chronic disorders. This was called a "tart" cell, which usually consisted of a monocyte with a secondary nucleus that apparently had been phagocytized. This same nucleophagocytosis also was noted in polymorphonuclear neutrophils. This cell is rarely a source of confusion to experienced observers.

Since the discovery of the LE cell in bone marrow, various tests have been developed using peripheral blood. Comparative studies have been done by many investigators, who now agree that the production of LE cells as seen in the various preparations of blood and bone marrow is an *in vitro* phenomenon occurring in the presence or absence of anticoagulants but depending on three elements, namely (1) the lytic, or LE, factor contained in the gamma globulin of the plasma, (2) nucleoprotein to react with the lytic factor and (3) active polymorphonuclear neutrophils to engulf the lysed material.

Clot Test for the LE Cell

One of the most satisfactory laboratory procedures for the demonstration of LE cells is the so-called clot test, as it has been demonstrated that formation of LE cells is enhanced by coagulation. The greater sensitivity of the two-hour blood-clot technique (to be described) as compared with results of examination of bone marrow should not be construed to indicate that the LE factor is in greater concentration in blood than in bone marrow. Two factors in the routine handling of

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bone marrow tend to limit formation of LE cells; these are the inhibition of clotting produced by use of heparin and the fact that preparations of smears usually are made within twenty minutes after aspiration.

Technique.—Venous blood (10 ml.) is withdrawn and allowed to clot for two hours in a clean glass tube. The clot is removed and placed on a special sieve made of stainless-steel wire gauze, 40 meshes per inch, fitting over a Petri dish. By means of a pestle, the clot is mashed through the screen, which removes the fibrin. A Wintrobe sedimentation tube is filled with the blood that accumulates in the Petri dish under the sieve. The tube is centrifuged at 2,000 r.p.m. for five minutes. Smears are made from the buffy coat after the serum is aspirated down to the layer of leukocytes. The smears are stained by Wright's method and examined for LE cells.

Comment

Although the procedure for making the LE preparations is relatively simple, their study should be done by a trained observer because certain difficulties may arise in the interpretation of results of the LE clot test. Histiocytes and, not infrequently, neutrophilic polymorphonuclear leukocytes may contain a secondary nucleus that has a sharp nuclear membrane, and there may be a relatively sharp differentiation between chromatin and parachromatin. This nucleophagocytosis ("tart" cell) is identical to that seen in bone marrow. As already indicated, such cells may be confused with LE cells by an inexperienced microscopist. LE cells found in the clot test are derived from mature neutrophilic polymorphonuclear leukocytes in the peripheral blood containing pale-purple intracytoplasmic masses of lysed chromatin. Lysis must be sufficient to impart a digested, smoky or ground-glass appearance. Such cells resemble in all respects the LE cells of bone marrow. In preparations made from clotted peripheral blood, clumps of leukocytes may be present at the edge of the smear. Some of the neutrophils in these clumps undergo distortion, which results in nuclear disintegration resembling the lysis of nuclear material seen in LE cells. One must be careful not to mistake damaged polymorphonuclear neutrophils for LE cells.

Small aggregations, or rosettes, of polymorphonuclear neutrophils are frequently seen in preparations containing LE cells. These rosettes should be distinguished from the clumps of leukocytes just described. Extracellular, pale-purple, amorphous, nuclear masses are often seen in preparations containing LE cells. The presence of rosettes and of free amorphous nuclear masses creates suspicion, but positive results of the test should not be reported unless true LE cells are seen.

In a correlation of the results of the LE clot test with the clinical diagnoses in a series of 347 patients, it was noted that the results were positive in all patients who had subacute to acute disseminated LE, whereas the results were negative in those who had chronic to subacute lupus erythematosus or discoid lupus erythematosus.

A small percentage of patients with rheumatoid arthritis have LE cells in the clot test. Also, certain patients receiving hydralazine (apresoline) hydrochloride for hypertension may present symptoms not unlike those of LE, and clot tests may reveal LE cells. When use of the drug is discontinued, the symptoms clear up and the LE cells disappear from the clot test, although such disappearance may lag behind the clinical improvement.

LE cells have been reported by some workers in disorders such as periarteritis nodosa, dermatomyositis, hyperglobulinemia not related to LE, pernicious anemia and reactions to drugs. Other workers have been unable to find LE cells in these conditions.

The consensus is that the LE clot test is a valuable laboratory aid in the diagnosis of lupus erythematosus. The test cannot be used for prognosis in spite of the fact that the cells may disappear during remission. There are factors regarding the sensitivity of the test that are not clearly understood at present. Results of the clot test may be negative in an occasional case of acute disseminated lupus erythematosus.

Editorials

JOHN F. BRIGGS, M.D.
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HENRY G. MOEHRING, M.D.

FREEDOM FOR PHILANTHROPY

Freedom to exercise one's will is a right which men have fought to exercise—and when lost, fought to restore—since time immemorial. We, as Americans, are engaged today in such a struggle to retain that elusive quality, most often called "liberty," on many fronts.

This may seen an unusual introduction to a discussion of independent vs. federated fund-raising for health and welfare agencies. Yet, to many, free will is the heart of the question.

Philanthropic giving is a unique characteristic of this country. In no other nation have private citizens rallied to support medical research and provide aid for the handicapped and unfortunate on the scale that we have achieved. In other countries, where such programs are carried on at all, they usually become a function of governmental agencies supported through taxation. Any step which may threaten this desirable American tradition should be taken cautiously.

Which agencies one should support is a question that no person can answer for another. Each individual differs in his approach to a given cause. Some may think one far more worthy than another—and give in that ratio. Some, through personal experience, may feel that an agency is not worthy of his support. That is, and should be, his decision to make.

If an agency cannot or does not impress the public with the merit of its cause, that agency should not be supported long. Thus, free will as expressed by the public becomes a "police force" for weeding out groups which do not merit support or duplicate the work of other agencies.

In the case of the so-called "federated" or "united giving" plans, the expression of one's free will is easily dissipated. By default, the individual's decision as to which agencies he will support and in what amounts, is all too often passed on to others. Thus, the very heart of philanthropic giving is touched.

Philosopher John Dewey once observed that we should not destroy one institution, in this case—philanthropic giving, unless we are certain we replace it with one that is superior.

Independent thinking is a painful process, no matter how educated the person. It is much easier to be persuaded by catch-phrases or appealing rationalizations than to think a problem through.

Before you, as a practicing physician and a leader in the community, make a decision concerning independent vs. federated fund-raising, satisfy yourself that you have the correct answers to the following questions—just a few of the many involved:

1. Do you decrease the number of agencies by pooling them into a single fund drive? Or the total amount of the funds sought?
2. Why, if combined fund-raising is a panacea, are there so many federated drives in this state experiencing difficulty in maintaining adequate public support?
3. Isn't it possible to budget the support for health and welfare agencies as one would do in his home or business and reduce the irritation of haphazard giving?
4. Are the individuals who control federated funds elected in a manner consistent with democratic principles?
5. Do you favor such a socialized approach to the solution of our community and national problems?
6. Are the reasons for conducting such a plan strong enough to warrant the action?

The question of independent vs. federated fund-raising may be troublesome—but not a menace. The loss of freedom to exercise one's will is!

G. RAY HIGGINS,
Executive Secretary
Minnesota Heart Association

FAMILY SERVICE—WHAT IS IT?

Across the United States and Canada, in every city of any size, there are Family Service agencies. Altogether, there are 245 of these agencies, if we include those in Alaska and Hawaii. Approximately 45 per cent of the entire population of the United States is accessible to this service.

Family Service agencies are members of the Family Service Association of America and must

First editorial in a series on "Family Service."

meet required standards which include: A staff of trained social workers, most of whom have a master's degree in Social Case Work; a lay board serving without pay; adequate financing from private funds; proven ability in offering skilled case work to families and children. In addition, statistical reporting must be uniform so that valid comparison between agencies and communities can be made.

In Minnesota, five agencies meet these qualifications. These are: The Jewish Family Service of Saint Paul and Minneapolis, and the non-sectarian Family Service of Saint Paul, Minneapolis and Duluth.

The historic background of many of these agencies is similar. In Saint Paul, Family Service began in 1892 as the Associated Charities, for coordinating voluntary relief. Later, it became the United Charities, and tried to work on the cause of poverty while still giving financial aid. Now, as Family Service, its responsibility is to help families with social and personal problems make the best use of their own and community resources, so that they can live full and satisfying lives, and raise happy, well-adjusted children.

Tensions arising out of personal relationships are the most common cause of application for our service. Marriage partners who have lost their direction and find themselves growing apart; parents who no longer understand their children and who are concerned because their children are no longer in harmony with them; emotional problems which interfere with social well-being—these problems, or some aspect of them, are the area that Family Service agencies are prepared to serve.

The case workers in Family Service agencies are in a position to see the effects of illness, both physical and emotional, on the entire family, and also to see the effects of family tension, as they aggravate physical and mental illness. For this reason, family agencies and physicians have much in common and can often be mutually helpful by working together for maximum use of both resources in helping families with problems.

As a private non-sectarian family agency, people of all religions, races, and economic and social levels, are eligible for service from Family Service of Saint Paul. The only requirement is that they live within the area which supports the Greater Saint Paul Community Chest which raises the funds that support the service.

In order to help with the often complicated and diverse family needs, special services have been developed which include foster care for children, homemaker service, financial and home management counseling and others, which will be described in later issues. The Family Service of Saint Paul welcomes this opportunity to make its service better understood by the medical profession. The family agency and the physician can both give greater service if they understand and work together for the benefit of man.

DAWSON BRADSHAW, *Executive Secretary, Family Service of Saint Paul*

STALL THE EXECUTIVE HEART ATTACK

While walking in a cemetery recently, I came upon the ornate head stone of an executive friend of mine. He had died recently from overwork. This was the inscription.

> "Here lies Joe,
> A nice guy to know.
> He couldn't get his people doing
> Work without his always stewing."

Yes, lots of executives stew about their men. "Why don't they handle responsibility?" "Why don't they carry through?" "Why don't they plan?" "Why don't they get things done?" And it's this stewing—this feeling of having personally to stay on top of every detail all of the time—that gradually exhausts the executive.

But how do you get men to do a job? How do you get them to do it without overburdening the executive?

Delegate Details—We often find executives stewing over details that other people should handle. I remember a president who was doing detailed accounting and credit work. Another president was passing on all buying. The net result—they had less time for planning and stimulating men. As a consequence, problems were constantly coming to their desks. They were working twelve to fifteen hours a day.

Get Men to Plan.—All too often, an executive hasn't forced planning down the line onto his men. He has permitted them to bring all planning up to him.

For example, a sales manager should be forced to plan his territories in such a way that he can meet competition. If he comes in crying, "Competition is getting rough," and gets by with it,

he has simply dumped all his problems on his boss's desk. The executive who permits this starts worrying about things that he really should have others handle.

Let "Them" Do It.—Sometimes a company is afflicted with "committee-itis"—all executives are in one committee meeting after another. Endless time is spent trying to get things done through committees. The difficulty with this is that committees generally don't take responsibility. In addition, they often develop into buck-passing bodies. What happens? More and more problems come up to an executive's desk. It was assumed the committee would handle them. But no one in the committee took real responsibility!

A firm may have a management committee, sales committee or a special production committee that reviews every little problem, but no one takes any real action. Key people spend a lot of time in meetings. But problems are still dumped in the lap of an executive for him to worry about. *And* other people could easily have solved the problem!

Oh, For a Staff in Time.—As a company grows it becomes evident that staff people are needed in addition to line. (Ordinarily, we would define a staff man as "anyone who has to get something done for the company through someone else who doesn't report to him." For example, personnel people, cost accountants, production control men, and market research men would be staff. Salesmen, production operators, and foremen would be line.) It's easy to set up one staff position after another. Very often, the need for the staff people isn't really there. The line could have handled it. *But every time you add a staff person, you add more problems of co-ordination.*

Sometimes the staff people are needed for a temporary problem, but after the problem disappears, the staff carries on. These staff people, then, look for things to do to justify their existence. Generally, they look in other people's bailiwicks. This usually leads to trouble. And where does this trouble come home to roost? Right on some executive's desk! And so he has one problem after another trying to solve conflict between staff and line.

Often staff people start taking over responsibilities that belong to the line. The line, then, won't take responsibility. For example, the personnel department may handle employe problems. The inspection department may relieve foremen of quality problems. The market research department starts to relieve sales managers of sales planning. This leads to weak line people and usually to poor operation. The staff people actually *cause* more and more problems, because the line people have relaxed their own attention to them. This results in more problems coming up to the executives, problems that could have been solved by men below them.

You Can Prove It with Figures.—As a company grows, it may easily succumb to a creeping paralysis of figure men. One report after another is developed, because it's "essential" to the business. Each of these reports goes to the executive's desk. This forces a lot of reading and concentration on his part to study them. In addition, these record keepers get in the hair of the other people by demanding so much of their time for making up reports. All of these things add to the problems of co-ordination of the executive.

How should you set up record keepers? Each record man should be responsible, not for records, but for getting some constructive action in the company as a result of the records. You then find that you relieve the executive considerably. You force the records to produce value. You help prevent their excessive growth. And you force the records to go to subordinates to make decisions. Without this you have an added burden for the executive—something else to stew about.

"You've Got Full Authority."—Too often, people assume that simply saying, "You've got full authority" solves all problems of authority. Many an executive worrying about the fact that men don't take responsibility has fallen into this trap. But authority is a very complex thing. It means nothing unless the man "feels" that he has it. What does authority mean? It means the right to make minor mistakes and to make them individually with impunity. In this connection, we suggest the rule of errors:

> "If a man has responsibility for a result, he should be allowed to make the necessary decisions *and the normal errors* that those decisions might result in in arriving at that result."

Too often, an executive has become concerned about every little error that people make along

the way. He calls these to the attention of the man. As a result, nobody will stick his neck out and take any action. Things don't move. In other words, he has not really given authority.

Authority really means the right to make some errors. Actually, the executive that does not allow his men to do this starts stewing about every little error that comes along. Once he realizes the importance of the rule of errors, it becomes much easier for him to tranquilly accept the little things that go wrong along the way.

Make Them Accountable.—The very life blood of an organization is accountability. Very often, the reason a very fine set-up doesn't work is that people individually are not accountable. In other words, individual men do not get credit or discredit if certain results are or not achieved.

When you don't have accountability, you develop an excessive burden on the executive to keep pushing and pushing to get things done. This alone can easily result in pushing the executive beyond his powers or his energy. Problems occur because people have been allowed to make decisions without being accountable for them.

For example, the sales department may be allowed to exert a great deal of pressure to get research done on crackpot ideas but not be accountable for the cost of that research. But the executive is! Perhaps a superintendent does not feel accountable for costs, but the executive at the top is quite concerned about the cost trend in his company. Until the superintendent is held accountable for the cost of operation of the plant so that he feels that it's his job to keep it actually in line, there is just one more item for the executive to worry about.

This also applies in product development departments. Development men love to turn out a beautiful "well-engineered" product. But perhaps it's one that will sell for $30 when the market will only take a $15 item! Until you make the development man accountable for producing a product that can be made at a salable price, you find you have numerous problems of co-ordination in production, sales, and development. This adds to the already heavy burden of the executives at the top.

Let's Make Men Successful.—Many executives haven't developed the spirit in their organizations that it's the job of every supervisor to make his men successful. To the extent that an executive permits men to pass the buck downward, people do not take responsibility. Duds show up. Action isn't taken. He should establish the attitude in the company that it's the job of every supervisor to make his people successful, and that a man's failure is probably the supervisor's fault. He will then get better action down the line. Fewer of the problems have to come up to the executive.

How Many Can You Supervise?—Too many executives want to keep their fingers on everything. They're in constant turmoil trying to keep in touch with all angles of the business.

For example, I know of a president who had fifteen people reporting to him. People had to stand at the door waiting to get in. This put excessive pressure on him. He had so much to do that it was hard for him to keep on top of everything. He had to put in long hours in order to supervise his men. At that, he did it poorly. Problems were always popping up. He became a worry wart.

Keep Your Balance.—One of the most difficult principles for an executive to follow is that of balance. In other words, he must constantly put pressure on all functions to be sure they're all coming along. Otherwise, one will outstrip the other and problems will develop.

For example, one company put a lot of effort into sales, and it was productive. The only trouble was that competition was developing new products and production methods to such a point that this company was not competitive in price. This president was at his wit's end trying to keep his company afloat.

I know of another company that put all of its eggs in the plant production basket. This was fine! They kept costs down! Then sales dropped 35 per cent. Little effort had been put into sales. It wouldn't help to tell this president not to worry. With a 35 per cent drop in sales, what president wouldn't worry?

Often executives don't realize that some pressure on all functions is better than excessive pressure on any one at any one time. When a president gets the right balance of effort in all of the functions under him, he usually finds he can operate in a much more relaxed way. All

areas of the company go ahead. He isn't caught short nearly so often.

These are only a few of the management problems that lead to excessive worry and stewing on the part of an executive. They lead to low production, high waste, and trouble. And it doesn't do any good to tell an executive, "Don't worry." He has to worry, or he feels he has to. He's got problems. But if he learns to straighten out these problems by following good management and organization principles, he finds that he can relax. He can plan better. The cogs of the organization are meshing. The whole company goes ahead on a smooth, easy basis, and the executive, himself, is able to find time to relax and to play a little golf.

EDWARD C. SCHLEH, *President*
Schleh Associates
(Management Consultants)

UTILITIES AS AN INVESTMENT

"Who owns the electric utilities?" is a question that is asked every utility executive many times and is the subject of a great deal of popular misconception. We believe that the answer to that question is good evidence of the standing of utility securities for investment purposes.

The electric utility industry in the United States is owned by approximately 3.7 million stockholders who, of course, are direct owners. They come from every walk of life including doctors, lawyers, merchants, farmers, laborers, office workers, teachers and housewives. Nearly every American has an indirect financial interest in the electric utility companies. There are, of course, also thousands of individuals who own bonds, debentures and notes of electric utilities who could be classified as direct owners. The 90 million life insurance policyholders and the more than 20 million depositors in mutual savings banks are examples of such indirect ownership, let alone those interested in pension funds, fraternal organizations, religious and educational institutions, and others that are heavy investors in utilities.

The Institute of Life Insurance points out that the nation's life insurance companies have nearly $13 billion invested in the securities of public utilities, and from that investment the policy holders are drawing about $400 million annually in interest and dividends going toward the enhancement of the value of their policies, the payment of dividends on their policies, or defraying the cost of their insurance. The Institute also shows that the $13 billion utility investment is the equivalent of nearly one-third of the total assets of all privately owned electric, gas, telephone and telegraph companies in the country; and that the long-term bonds, debentures and notes of such public utility companies owned by the life insurance companies represent two-thirds of such securities of all of these companies now outstanding.

As a general rule, all of the utilities of the United States have experienced a sound and steady growth for many years. As the electric light and power utilities represent by far the largest segment of the public utility industry, and as that segment is the part of the industry which I know best, I shall confine the rest of my remarks to the electric light and power companies.

This industry is only seventy-five years old, and during all that time it has supplied good service and stayed ahead of the electrical requirements of its customers. It has successfully withstood the rigors and trials of two world wars, several depressions, and a period of years when the government itself seemed bent on "duplicating it" out of business. The industry now stands in full stature, with an enviable record of continually improving its efficiency of operation, paying a heavy load in taxes, and continuously reducing the average cost per kilowatt hour for service to its customers.

Since World War II, the electric industry has grown at a rate that doubles itself every ten years and present indications are that it will do so again in the next ten years.

Although the federal government has expended many millions of public funds for investment in electric generating facilities, it still supplies only about 13 per cent of the total electrical requirements of the nation. We have enough faith in the American system and in the American people to believe that they will not permit our industry to be destroyed or duplicated out of business.

The privately owned electric utilities are taking an active part in studies looking toward development of a cheap and reliable method of using nuclear fuel for the generation of electricity and will be quick to convert to this new type fuel once it is convinced it is cheaper than other means

of generation. In our opinion there is no reason to be concerned about the obsolescence or replacement of present electric generating plants because of developments in the utilization of atomic energy in the generation of electric energy because it will only replace present fuels used for that purpose. About 83% of the present investment in a utility plant would still be required and we believe the change over, if it ever comes, will be so gradual that it will not materially affect the useful life of present or conventional plants.

It therefore appears that the electric light and power industry should continue to prosper and provide fair earnings for the payment of interest and dividends on the monies invested in its securities. The future looks good.

ALLEN S. KING, *President*
Northern States Power Company

THE PRESENT STATUS OF THE BALLISTOCARDIOGRAPH

Interest in the ballistocardiograph as a diagnostic tool has increased rapidly since the end of World War II. There are now available at least three monographs[1-3] describing the several kinds of recording apparatus and giving clinical experience. Approximately 300 papers have been written on the subject since 1947. This interest in the ballistocardiograph is justified in part because it measures something related to the power or strength of the cardiac muscle[4] and therefore is concerned with a component of cardiac function which is not measured by the electrocardiogram or any other tool of the cardiologist.

The ballistocardiogram may be recorded with the patient lying supine on a moving bed which may, or may not, be restrained with springs.[5-9] or the patient may be on a fixed bed and the motion between the patient and the bed may be recorded.[10] A major problem is presented by the fact that the dorsal tissues have elastic and damping properties which impose distortions on records taken with both the popular direct body recording introduced by Dock and with bed systems restrained to a significant degree by springs.[11] A system has been recently designed which appears to have overcome most of these difficulties,[8] but this instrument has not been studied in the clinic. Ballistocardiography is currently going through a phase of instrumentation development which will not be over for some time.

In spite of the fact that records obtained with spring-restrained beds and the direct body pick-up devices contain important distortions both of amplitude and of timing, a great deal of useful information has been accumulated with these instruments. Starr[4] and his associates studied the effects of ejecting known quantities of blood of different rates into the aortae of warm cadavers. It is possible to produce both normal and abnormal ballistocardiographic patterns. This work demonstrated that abnormal ballistocardiographic wave forms *may* be produced by "weakness" of cardiac contraction. However, one should not lose sight of the fact that extracardiac factors, such as changes in the elastic properties of the large vessels and the tendons which anchor them, have not been properly evaluated. Heart disease, in which the myocardium has been damaged, is usually associated with abnormal wave forms and/or low measurements of force (usually computed from the IJ limb). In the case of conges-

From the Laboratory of Physiological Hygiene, University of Minnesota, School of Public Health, Minneapolis, Minnesota.

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tive heart failure, abnormal patterns have been shown to improve with treatment and general improvement in the patients condition. However, the only abnormal pattern that appears to be diagnostic is that associated with coarctation of the aorta. Much work has been done on coronary heart disease where a high incidence of abnormal wave forms has been found with the use of the high frequency (Starr-type) bed and with the Dock apparatus. When groups of male coronary disease patients are studied with the low frequency critically-damped bed of Nickerson, the coronary groups are found to have mean IJ force values which are substantially below the mean of "healthy" men of the same age.[12] There is, however, a large overlap of values between the normal and coronary group. Study of the normal male population shows a striking decline in the IJ force with age, regardless of the method used to study it,[13-15] and a marked increase with age in the numbers of the otherwise healthy individuals who have apparently abnormal patterns obtained with either the high frequency (Starr-type) bed or the Dock body pick-up apparatus.[13,15] For example, in 174 businessmen, aged fifty to fifty-nine, who were studied in this laboratory with the high frequency (Starr-type) BCG, only 44 per cent were judged to have normal patterns. This fact places a very heavy burden of proof on the ballistocardiographer who suggests that an abnormal wave pattern in an otherwise normal individual has prognostic significance and makes current ballistocardiographs almost useless, as far as identifying significant coronary disease in the middle aged male is concerned. The interpretation of an abnormal pattern in an otherwise healthy individual is one of the major problems facing ballistocardiography today.[16] Until this problem is solved, the clinical usefulness of the ballistocardiogram taken with any of the instruments in common use will remain extremely limited.

It is much too early to give a final judgment on the value of the ballistocardiograph to the clinician. Much work remains to be done. The current improvements in instrumentation must be evaluated in the clinic. Detailed physiological studies must be carried out to describe the magnitude and type of errors which arise in the transmission of force through the internal network of tissues. In the meantime, there is evidence to support the concept[17] that the study of groups of individuals with the spring restrained models which are in current use will yield information which is of value to the clinical investigator.

HENRY LONGSTREET TAYLOR, Ph.D.

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REINSURANCE IS NOT REASSURANCE

The old bogey-man, M. M. Davis, is on the loose again larruping the medical profession with might and main in his latest work entitled "Medical Care for Tomorrow," a book which regardless of one's views is packed with information. Dr. Davis has been known to many of us for years, to quote Albert Deutsch, as ". . . the unrelenting gad-fly on the back of the AMA mule." That the American Medical Association isn't completely mulish is shown by the fact that where it once objected to voluntary health insurance, it is now aggressively in favor of it. Dr. Davis is equally unmulish, as may be seen by his change of view. As a member of the Committee on the Cost of Medical Care back in 1932, he was against compulsory health insurance; now he is for it.

Sheer stubbornness is one thing; intelligent objection to a proposal is another. An unchallengingly negative attitude is not enough, and yet to object intelligently one must have sufficient knowledge to spot errors or misleading statements in the other's argument. There is much opposition in medical circles to federal reinsurance, and an understanding of Oveta Culp Hobby's plan requires more space than is available here. It may be briefed, however, in Mrs. Hobby's own words as follows:

"If the XYZ Insurance Company decides it does not want to assume all the risk in this fleet of cars, it may—by paying a fee—assign, or in other words rein-

sure, part of that risk with another insurance company or a group of insurance companies. In this way, should the insured fleet have excessive losses, the XYZ Insurance Company's liability would have been substantially reduced. This is straight reinsurance. . . . How do the terms apply to the federal insurance proposal? The proposal specifies that before the federal fund is liable for any claims, a reinsurance company must itself assume some loss above and beyond that anticipated in the calculation of its premiums. . . . A company can, by reinsuring with the federal reinsurance service, spread the risk of excessive aggregate losses in the same way as does the XYZ Insurance Company, which I have used as an illustration. The reinsurance proposal is not a subsidy. And it is not, of course, compulsory."

This all sounds quite plausible and convincing and no doubt it is true. However, there is another side to the matter. Read what Mr. Edwin J. Faulkner, president of the Woodmen Life and Accident Company, has to say:

"Advocates of the measure (federal reinsurance) have noted the considerable contribution made to the development of life insurance, fire insurance, and other lines by adequate reinsurance facilities and, noting further the relatively small volume of health insurance business done, have argued that expanded reinsurance facilities in this field would have a stimulating effect. Such a conclusion can proceed only from a misunderstanding of the essential function of reinsurance, which is the spreading of risks larger than the initial insurer is willing to carry. It is true that in life insurance, for example, reinsurance makes it possible for an insurer to assume larger risks than it could without reinsurance. Here there is almost never a concentration of risk large enough to require spreading a potential loss. Even with catastrophic or major medical expense insurance, which presents the maximum amount of risk usually found on one life, the insurer's potential loss is seldom as much as $10,000, a sum well within the capacity of all but the smallest insurace company to carry alone."

He also says:

"Reinsurance can distribute losses among insurers just as insurance distributes that among policy-holders, but no matter how far this distribution is carried, it must be sound to succeed. Reinsurance does not increase the ability of the insurer to sell protection to the unwilling buyer. Reinsurance does not reduce the cost of insurance. Reinsurance does not make the insurance available to any class of risk or geographic area not now within the capabilities of voluntary insurers to reach."

Mrs. Hobby views with alarm the fact that in 1948, $6.6 billion of total medical expense were not covered by insurance and that by 1953, $8.0 billion were not covered. There was thus an increase in the amount uncovered of $1.4 billion. That this is true, there is no question. It is also true, however, that $6.6 billion represented in 1948 92 per cent of the total medical bill, while $8.8 billion in 1953 represents about 80 per cent of the total. This might even be considered by some as an improvement. The percentages themselves are high, because the total medical expense figure used admittedly includes a large amount which under no conceivable insurance plan would be covered.

A recent editorial in one of our daily papers states:

"The in-between middle class does not have the means to meet such costs (catastrophic illness) without hardship, and cannot at present get adequate protection."

It is, of course, true that the large group making up the so-called middle class consists of all variations between the moderately affluent and those in extremely straightened circumstances. To say at once that catastrophic insurance is not available to all or any of this class, is simply not true. There are forty companies in this country writing catastrophic insurance, with 1,500,000 persons covered. I have before me a policy submitted by one of the largest insurance companies in America, offering medical protection up to $5000, with the first $300 of expense deductible, for a man eighteen to thirty-nine years of age, together with his wife and a son and daughter, for $53 a year. It may thus be seen that this type of insurance is not only available but also accessible to millions who do not bother about getting it. With twenty-five million television sets throughout the land, the cost above-mentioned does not appear to be exorbitant.

HAROLD E. HULLSIEK, M.D.

PSYCHIATRIC OUT-PATIENT TREATMENT

(Continued from Page 635)

a minimum or reasonable fee if required (Question VI).

6. 90 per cent of the respondents indicated that they would return willingly or be eager to return to the Center in the event of future psychiatric difficulty (Question VII).

7. 72 per cent of the respondents indicated they are well and healthy or bothered only occasionally by their condition; 18 per cent have received additional help from other non-psychiatric sources and 5 per cent have sought further psychiatric help (Question VIII).

8. 3.8 per cent have been hospitalized (Question VIII).

Reference

1. Kram, Charles, and Berkwitz, N. J.: Patients' impression of a community mental health center. Minnesota Med., 36:591-593, 1953.

President's Letter

SOCIAL SECURITY FOR PHYSICIANS

Your officers and councilors are frequently asked why the House of Delegates of the AMA has recently voted to oppose the inclusion of physicians in the Old Age and Survivors Insurance Program, except on a voluntary basis. A wealth of material has been published in *The Journal of the American Medical Association,* both editorially and by Dr. Frank G. Dickinson of the AMA staff, and we all should be well informed on the subject if we take time to read the material available. However, I suppose the pressure of time has led many of us to neglect what should be compulsory reading and study. Dr. Walter Judd, a member of the Congress of the United States, recently wrote to me that he was surprised at the number of letters he received from doctors, urging that they be included under the social security program.

The subject of social security is particularly important to members of the medical profession. It is for this reason that the AMA has strongly supported the Jenkins-Reed-Keogh bills, which have appeared in various forms in Congress during the past sessions. These bills would establish a voluntary retirement plan for the self-employed and the pensionless-employed. They would amend the internal revenue code, but would not change the Social Security Act. They are in the public interest. The amount of each person's pension would be determined by how much he set aside for old age, and not one penny would be added to his fund by the Government. He would be permitted to defer taxes on the annual amount set aside each year until he retired and began to receive his pension, which would be currently taxable. The provision of these bills for tax deferment until retirement are a counterpart of those now enjoyed by employed persons covered by more than 20,000 tax-exempt pension plans. Dr. Dickinson has repeatedly pointed out in committee hearings in Congress that without such tax deferment, physicians are discriminated against.

Opposition to the trend toward the Welfare State might be called the fundamental reason for the opposition of the AMA to the extension of the Old Age and Survivors Insurance Program.

An ostensible reason for physicians to disapprove compulsory coverage OASI warrants only a brief comment. The median age at which self-employed physicians over age sixty-four are currently retiring is seventy-four. The retirement age of self-employed lawyers, dentists, farmers is probably about the same. Under the so-called work rule, no eligible person can draw Old Age and Survivors Insurance Pension if his earnings are over a stipulated amount. This would obviously mean that half of the self-employed physicians, under the President's proposal, would be required to pay social security taxes but not receive one penny of benefits until

age seventy-four. But relaxing the work rule to make coverage more attractive to these ten million gainfully employed would, unless accompanied by a sharp increase in the OASI taxes, merely increase the get-something-for-nothing potential of the Act.

The basic objection to bringing an additional ten million persons under the OASI is that such an action by the Congress would be another long step toward big Government and the Welfare State. Social Security taxes, counting both employers' and employes,' are currently only token payments, and will defray only a portion of the costs of the OASI pensions. The tax rates of employers and employes should be doubled, and also graduated according to age—a change that is much more urgent than modification of the work rule. The unpaid balance of the pension cost as older persons receive their monthly pension checks must be paid by another generation.

Those who oppose the steady march toward the Welfare State must also refuse the bait—in this case pensions at cut-rate prices. They must oppose the doctrine of individual irresponsibility, except for the care of those in dire need, which, in fact, is the essence of the principles that guide the life of a physician in his practice. They must stand firmly against the exploitation of youth by those who were born many years earlier. They must insist on standing on their own feet and providing their own retirement needs. Those who can pay should pay their own way, those who cannot pay must, of course, be helped. It is apparent to students of our Federal social security system that some change in the present mechanism is necessary in order to show plainly to the entire country what the real cost of the existing level of benefits is, and then to have the present generation of the working population pay the full cost of the system in the same way we expect the next generation to pay its costs. There is every reason to believe that many advocates of the Welfare State are deliberately concealing the true cost of our Old Age and Survivors Insurance Program, in order to foist a much greater Federal system on the country before the people wake up to its real nature and cost.

Arnold O. Swenson

President, Minnesota State Medical Association

Medical Economics

Edited by the
Committee on Medical Economics,
Minnesota State Medical Association
George Earl, M.D., Chairman

HEALTH REPORT ON STATE RELATIONS ISSUED

The report by the Commission on Intergovernmental Relations, submitted to the President on June 28, 1955, deals briefly, but sympathetically, with Federal assistance in public health projects, hospital construction, research and professional training programs. Dr. Franklin D. Murphy, chancellor of the University of Kansas and former dean of its medical school, headed the fourteen-member committee.

According to the report, the Murphy committee agreed that public health grants by Washington are wise and desirable, then set down certain fundamental principles. These principles are:

1. Primary responsibility for meeting health problems rests with the community;
2. Aid grants should supplement, not supplant, local effort;
3. Community need is the first criterion for grants-in-aid;
4. Federal help should be of temporary nature;
5. Assistance funds should be matched, but with flexibility of formula;
6. Evaluation program is essential.

The report is quoted in a recent issue of "Washington Report on the Medical Sciences," which states:

"The advisory committee recommended continuance at present level (about $57 million per year) of Federal grants to states for maternal and child health, tuberculosis, venereal disease, cancer and heart control, and general public health activities. It indorsed Hill-Burton hospital program but urged that voluntary health agencies be called upon for counsel before Congress grants this undertaking another extension (it is due to expire in 1957)."

The report further states that Federal financial support of medical research was heartily indorsed. In the matter of professional training, the committee recommended establishment of public health fellowships but warily avoided taking a stand on subsidies for medical schools, pending "an entirely objective study of this problem." Like the Hoover Commission and its medical task force, the Murphy committee favored creation of a Federal health council to co-ordinate.

CONGRESS ADJOURNS WITH HEALTH BILLS PENDING

The 84th Congress adjourned, leaving considerable unfinished business as far as health measures are concerned. Some issues, although they are lying dormant, will be considered by the second session which convenes in January. These issues include reinsurance of health insurance plans, guarantee of mortgages for health facilities and a series of bills dealing with U. S. grants-in-aid.

However, a recent issue of the AMA Washington Letter carried with it a special report of legislation status as the first session was nearing its close, and the actions taken are as follows:

Salk Vaccine

Many bills were introduced regarding control, distribution and use of biologicals. Last-minute compromise on these measurses provided $30 million to carry out the program of providing for inoculations of needy children.

Disability Insurance

This bill, providing cash benefits for disability, lowering the pension age for women and liberalizing the Social Security Act in other ways, was reported out of House committee and was passed by the House. Senator Byrd, chairman of the Senate Finance Committee which would consider the bill, is reported as being opposed to passage of this bill at this time, and would prefer a thorough study of the proposal before any action is taken. This will be an issue in the second session of Congress. The AMA is opposed to this legislation because (1) machinery at the Federal level to supervise the certification of disability would put the Government firmly in the middle of medical practice, and (2) pressures would be applied on physicians for speedy certifications.

Doctor Draft Extension

The doctor draft remains in effect another two years, until July 1, 1957. In the two major changes from the old act, the new law (1) lowers from 51 to 46 the age limit for call-up of physicians, and (2) provides that any physician rejected for a medical commission for solely physical reasons shall no longer be liable on reaching age 35. The $100-a-month special pay for physicians in uniform is continued for four years. The AMA has opposed extension. It feels that until this discriminatory law ends, firm steps will not be taken by the services to attract physicians to military medicine as a career.

Military Medical Scholarships

As a partial answer to military medical problems, the Defense Department proposed full scholarships for medical students. They would be obligated for three years' active duty if scholarship is a year, or five years if scholarship exceeds a year. This bill is still pending. The proposals are supported by the AMA but with three suggested changes: (1) a student not be approached by the military until fully matriculated, (2) no student so selected to receive any preferential treatment, and (3) number of scholarships in a school not to exceed 5 per cent of any year's class or total enrollment.

Military Dependents

Still high on the Administration's priority list is the plan for a broadened and uniform application of medical care for dependents of all servicemen. This care, within limitations of the military, would be provided in the main by uniformed physicians and military hospitals; where such care and facilities were not available, local physicians and resources would be called on. Progress has been slow, and this bill will await action until the next session.

The American Medical Association feels that the Defense Department's emphasis is in the wrong place. The Association says that in this country military dependents, like other civilians, should be treated by private physicians and in private hospitals unless these resources are inadequate. Then, and only then, should uniformed physicians and military facilities be employed. Also, the Association objects to the use of a special draft law to provide physicians to care for civilians within this country.

Federal Aid to Medical Education

Most prominent are identical House and Senate bills for a five-year, $250 million program of grants to schools for construction, expansion, modernization and maintenance. These bills have had hearings completed and await action until the second session. Up to two-thirds of new school construction cost would be supported by the Government, and up to one-half of existing school costs; if an existing school increased its freshmen enrollment 5 per cent over last year, it also could get up to two-thirds.

The AMA favors this measure in the belief that an emergency condition exists in medical schools. But it proposes dropping out the 5 per cent enrollment incentive and making certain that the advisory Medical Education Council include six "leading medical authorities" and specialists in finance and construction.

Mental Health Survey

This became public law and provides Federal grants totalling $1,250,000 to non-government groups for financing an extensive three-year survey of national mental health problems. The American Medical Association gave its full support to this bill.

Federal Employe Health Insurance

Most U. S. Civilian workers would be eligible for coverage. They would choose between (a) an over-all Federal plan, to be contracted for nationally by the Civil Service Commission, or (b) a local, employe or other type of plan. Major medical expense coverage also would be available. The U. S. would pay up to $1.50 per month for a single person, or up to $4 for one with dependents, or one-third of the premium, whichever is the smaller. Benefits that would have to be allowed are spelled out specifically in the bill. This bill was pending at adjournment.

Tax Deferments

Proposals for deferring taxation on money put into restricted retirement plans have been before Congress for quite some time. Generally they would allow physicians and other self-employed to pay income tax on the amounts when received

as annuity payments. The American Medical Association has pressed hard for this type of legislation. Hearings were completed on this legislation, but action will await the second session of Congress in January.

Bricker Amendment

Extensive hearings have been held on the resolution regarding the treaty-making powers of the President. The American Medical Association is a strong advocate in principle of the Bricker concept. This legislation is still pending.

PHS TO HANDLE INDIAN MEDICAL CARE RESPONSIBILITY

Effective on July 1 of this year, the United States Public Health Service took over responsibility for the medical care of American Indians, a duty that up to then had been performed by the Indian Bureau in the Department of the Interior. The program affects about 350,000 Indians living on reservations. Transferred to PHS from the Bureau are 3,600 employes and 970 buildings. Fifty-six hospitals, twenty-one health centers, thirteen boarding school infirmaries and numerous other health structures are included in the transferred real estate, which is estimated to be worth about $40 million. This was reported in a recent issue of the AMA Washington Letter.

According to the Letter, "the shift in responsibility is a result of legislation passed last year. It was supported by the Department of the Interior, the Budget Bureau and many medical groups, including the American Medical Association."

Personnel Continues

To handle the new task, the Public Health Service has established a Division of Indian Health in the Bureau of Medical Services. Dr. James R. Shaw, who has handled the program for the past two years on loan from PHS, will continue to direct it as chief of the new division. Dr. Frank French and Dr. Joseph Dean will remain as his top assistants.

TWO WORLD MEDICAL GROUPS DISCUSSED

A recent article in *The Journal of the American Medical Association* discusses two organizations which work toward world health, understanding and peace—the World Medical Association and the World Health Organization. The article was written by Drs. Harold S. Diehl, Minneapolis; Leonard W. Larson, Bismarck, N. D.; and Franklin D. Murphy, Lawrence, Kansas.

The two groups are "a team that is making one of the greatest contributions of our time to the improvement of mankind—a must for the prevention of the spread of communism," the article states.

An accompanying editorial states:

"Each country, of course, has its own problems, but there are many aspects of the control of disease and the providing of medical care that should be viewed internationally. Sometimes the view prevailing in one country is helpful when disseminated elsewhere. . . . Such value is readily apparent to everyone."

Goals Explained

The world Medical Association, a professional organization of physicians, developed an International Code of Medical Ethics, sponsored the first World Congress on Medical Education, and now is working in the field of world occupational health.

The World Health Organization, with 84 member nations, is within the general orbit of the United Nations, but administered separately. It has compiled and distributed information on many phases of health and disease; led in the control of malaria and yaws, and assisted in training thousands of persons from countries without health-training facilities.

The article states that the World Health Organization is valuable to the U. S. "both as an arm of foreign policy of our government and as a contributor to our domestic health." Both organizations have worked together, collaborating on projects and exchanging representation. "It is essential that these organizations continue to co-operate in order to assure the greatest possible competence," the article says. It concludes:

"The individual physician can help in developing understanding within his own community of the importance of the development of public health services in underdeveloped areas of the world as a barrier to the spread of communism."

In Memoriam

PERCIVAL HALE BENNION

Dr. Percival H. Bennion died June 30, 1955, in White Plains, New York, where he was visiting his daughter. Dr. Bennion retired from active practice in St. Paul in 1947.

Born in 1876 in Grove City, Minnesota, Dr. Bennion spent his boyhood in Litchfield. He graduated from the medical school of the University of Minnesota in 1902 and interned at St. Mary's Hospital in Minneapolis.

During his years of practice in St. Paul, Dr. Bennion was active in civic affairs. He was a member of the Midway Club, the Osman Temple of the Shrine, and on the Merriam Park library board.

Dr. Bennion was on the staff of Midway Hospital, a member of the Ramsey County Medical Society and a "Fifty-Club" member of the Minnesota State Medical Association.

He is survived by his two daughters: Mrs. Kenneth Huntzider, Miles City, Montana, and Mrs. Lester C. Tuttle, Winter Haven, Florida, and five grandchildren.

ALLOYS F. BRANTON

Dr. Alloys F. Branton, former Willmar physician and surgeon, died July 26, 1955, at the Baroness Erlanger Hospital in Chattanooga, Tennesse, where he had been administrator for nine years until his retirement a year ago because of illness.

Born in Minneapolis in 1895, Dr. Branton spent his youth in Willmar. He attended the University of Minnesota and graduated from the medical school in 1920. After interning at Minneapolis General Hospital, he affiliated with the Willmar Clinic.

Dr. Branton was president of the Central Minnesota County Medical Society and a member of the Minnesota State Medical Association. A specialist in hospital administration, he served as executive secretary and president of the Minnesota Hospital Association. He was a member of the American College of Hospital Administrators.

His many activities included a term as vice commander of the district American Legion, vice president of the Kiwanis International, and president of the Willmar Chamber of Commerce.

He is survived by his wife Helen T. Branton and two children: Alloys, Jr., of Philadelphia, and Mrs. Helen Wilhoit of Seattle.

HAROLD WILLIAM HAVEL

Dr. Harold W. Havel, former Jordan general practitioner, died July 23, 1955, in Omaha, Nebraska. He had been in practice there since 1949.

Dr. Havel was born in Montgomery, Minnesota, in 1909. He spent his boyhood in that town. He obtained his medical education at the medical school of Creighton University, Omaha, Nebraska, and interned in that city at St. Catherine's Hospital. After completing his training, he entered general practice in Jordan, Minnesota, in 1933.

While in Jordan, Dr. Havel was active in community affairs. He was president of the Jordan Commercial Club in 1939-40 and a member of the Knights of Columbus. He was president of the Scott-Carver County Medical Society in 1939-40, a member of the Minnesota State Medical Association and the American Medical Association.

He is survived by his wife and two sons, Thomas J. and Harold, Jr., of Omaha; his parents, Mr. and Mrs. T. N. Havel of Montgomery, Minnesota; two brothers, Dr. Thomas E. of Santa Monica, California, and Joseph of Glencoe; and two sisters, Mrs. John Petricka of Northfield and Mrs. Bernice Powers of Mankato.

HENRY EMIL ROKALA

Dr. Henry E. Rokala, physician of Virginia, died June 17, 1955. Dr. Rokala was born in Nashwauk, Minnesota, in 1903 and spent his youth there.

In 1924, Dr. Rokala graduated from Carleton College and for seven years taught at Shattuck Military Academy at Faribault. He then entered the University of Minnesota Medical School, graduating in 1937. He served an internship at St. Luke's Hospital in Duluth and then entered practice in Biwabik.

In 1941, Dr. Rokala established a practice in Virginia and remained there in practice until his health failed. He was a member of Phi Beta Pi medical fraternity, the St. Louis County Medical Society, the Minnesota State Medical Association, the Americal Medical Association, Virginia Lodge, Ancient Free and Accepted Masons, Royal Arch Masons, the Virginia Chamber of Commerce and a number of other civic organizations. He was a member of the First Presbyterian Church.

Surviving are his wife; two sons, Dwight and Curtis; a daughter, Winifred; and two brothers, John and Einar, both of Nashwauk.

STELLA LUCY WILKINSON

Dr. Stella L. Wilkinson, one of Minnesota's best-known women doctors, died July 22, 1955, at eighty-one years of age. She had been in poor health for two years.

Dr. Wilkinson was born in Vinton, Iowa. She attended Central High School in Saint Paul and the University of Minnesota, graduating from the medical school in 1903. She practiced in Duluth for many years, at Askov, Newport, at the Moose Lake State Hospital and the Faribault School. Two years ago, she retired from practice.

Dr. Wilkinson had been a member of the St. Louis County Medical Society, the Washington County Medical Society and the Rice County Medical Society. She was a life member of the Minnesota State Medical Association and received her "Fifty Club" certificate in 1953.

Dr. Wilkinson is survived by one sister, Mrs. Cordelia J. Crawford of Saint Paul.

Reports and Announcements

MEDICAL MEETINGS

National

Academy of Psychosomatic Medicine, 2nd annual meeting, Plaza Hotel, New York City, October 6-8, 1955.

American Association of Blood Banks, eighth annual meeting, Palmer House, Chicago, Illinois, November 19-21, 1955.

American College of Gastroenterology, annual convention, The Shoreland, Chicago, Illinois, October 24-26, 1955, followed by annual course in Postgraduate Gastroenterology, October 27-29, 1955.

American College of Surgeons, sectional meeting, Milwaukee, Wisconsin, February 27-29, 1956.

American Medical Writers' Association, 12th annual meeting, Hotel Jefferson, St. Louis, Missouri, September 30, 1955, followed by Workshop on Medical Writing, October 1.

Association of Military Surgeons of the United States, 62nd annual convention, Statler Hotel, Washington, D. C., November 7-9, 1955.

Endocrinology and Metabolism, 7th annual Postgraduate Assembly of the Endocrine Society, Indiana University School of Medicine, Indianapolis, Indiana, September 26-October 1, 1955.

Mediclinics of Minnesota, postgraduate course sponsored by Academy of General Practice of Broward County, Fort Lauderdale, Florida, March 5-14, 1956.

Mississippi Valley Medical Society, 20th annual meeting, Hotel Jefferson, St. Louis, Missouri, September 28-30, 1955.

National Society for Crippled Children and Adults, Palmer House, Chicago, Illinois, November 28-30, 1955.

Occupational Skin Problems, course sponsored by Institute of Industrial Health, University of Cincinnati, Kettering Laboratory, Cincinnati, Ohio, October 10-14, 1955.

Omaha Mid-West Clinical Society, twenty-third annual assembly, Hotel Paxton, Omaha, Nebraska, October 24-27, 1955. (see page xxv for program).

Venereal Disease Postgraduate Course, 24th session, sponsored by University of Chicago and Public Health Service, University of Chicago, September 26-30, 1955.

Winston-Salem Heart Symposium, Robert E. Lee Hotel, Winston-Salem, North Carolina, September 30, 1955.

State

Michigan State Medical Society, Pantlind Hotel, Grand Rapids, Michigan, September 26-30, 1955.

International

International Symposium on Enzymes: Units of Biological Structure and Function, Henry Ford Hospital, Detroit, Michigan, November 1-3, 1955.

MINNESOTA ACADEMY OF GENERAL PRACTICE

The Minnesota Academy of General Practice will hold its Fifth Annual Fall Refresher at the Radisson Hotel, Minneapolis, on Wednesday, October 19, starting at 8:30 A.M.

Eight hours of concentrated instruction will be given by fourteen authorities, highlighted by a talk by E. H. Rynearson, M.D., Rochester, Minnesota, at the noon luncheon. Also appearing will be Bert Seligman, M.D., Toledo; Gene Stollerman, M.D., University of Chicago; and George Logan, M.D., Rochester, Minnesota.

There is no registration fee, but a five-dollar luncheon ticket is required. Registrations are advisable and should be made through James A. Blake, M.D., 15 Ninth Avenue South, Hopkins, Minnesota.

WORKSHOP IN MEDICAL WRITING

A Workshop in Medical Writing will be held on the second day of the twelfth annual meeting of the American Medical Writers' Association under the instruction of members of the journalism faculties of the University of Illinois, University of Missouri, and University of Oklahoma, Saturday, October 1, 1955, from 8:00 a.m. to 12:00 noon at Hotel Jefferson, St. Louis, Missouri.

CONTINUATION COURSE

The University of Minnesota announces a continuation course in *Fractures for General Physicians* which will be held at the Center for Continuation Study from November 21 to 23. Management of the fractures most commonly seen in general practice will be stressed. The course will include a demonstration session, and registrants will be invited to bring x-rays from their own practices for consultation with members of the course faculty. The course will be presented under the direction of Dr. Wallace H. Cole, Professor, Department of Surgery, and Director, Division of Orthopedic Surgery, University of Minnesota Medical School.

INDUSTRIAL HEALTH COURSE

A postgraduate course in *Modern Considerations and Methods in Handling the Lead Problems in Industry* will be presented during the week of November 7-11, 1955, by the Kettering Laboratory in the Department of Preventive Medicine and Industrial Health of the University of Cincinnati. Physicians and industrial hygienists who are concerned with the lead problem and who are interested in attending the course should write for an application blank to Secretary, Institute of Industrial Health, Kettering Laboratory, Eden and Bethesda Avenues, Cincinnati 19, Ohio.

AMERICAN CANCER SOCIETY

The American Cancer Society has announced that its program of clinical fellowships, which was begun in 1948, will continue through the next institutional year, July 1, 1956, to June 30, 1957, with fellowships commencing July 1.

CRIPPLED CHILDREN CLINICS

The remainder of the fall clinic schedule conducted by the Minnesota Department of Welfare, Crippled Children Services, is as follows:

City	*Date*	*Place*	*Counties*
Crookston	Oct. 8	High School	Norman, Polk
Marshall	Oct. 15	East Grade School	Lac qui Parle, Lincoln, Lyon, Redwood, Yellow Medicine
Little Falls	Oct. 22	Charles Lindberg School	Morrison, Mille Lacs, Todd
Virginia	Oct. 26, 27	City Hall, Health Dept.	St. Louis, East Range
Hibbing	Nov. 9, 10	Village Hall	St. Louis, West Range
Willmar	Nov. 19	High School	Chippewa, Kandiyohi, McLeod, Meeker, Renville, Swift
Anoka	Nov. 22	Lincoln School	Anoka, Chisago, Hennepin, Isanti, Kanabec, Ramsey, Sherburne, Washington, Wright

PULMONARY-FUNCTION TESTS

(Continued from Page 601)

in the evaluation of right-to-left shunts (pulmonary hemangioma and certain congenital cardiac defects) and occasionally contributes to the differential diagnosis of primary and secondary polycythemia.

For assessing hypercapnia, no method is both simple and entirely satisfactory. Determination of the carbon dioxide-combining power of venous blood is a test that is widely available but that in itself cannot distinguish between respiratory and metabolic disturbances. It is well to remember that elevated values for the carbon dioxide content of blood accompany both metabolic alkalosis and respiratory acidosis. The accurate definition of certain disturbances of acid-base balance occasionally requires direct chemical analysis of arterial blood.

In recent years, there has been rapid advancement of knowledge of both normal and abnormal pulmonary physiology. Much of this has been obtained with complex techniques which are currently impractical for routine clinical use and which have not been presented here. More extensive discussions and bibliographies may be found in the accompanying list of review articles.

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Woman's Auxiliary

MESSAGE FROM THE PRESIDENT

As our activities begin this fall, I bring greetings from your new officers. We pledge to you our support and it will be our pleasure to serve you in every way possible.

It was my privilege to attend the 32nd Annual Convention of the Woman's Auxiliary to the AMA, which was held in Atlantic City, June 6-10. Minnesota was well represented, with eleven delegates. Stimulating reports of officers, chairmen, and state presidents, gave evidence of the excellent work that has been accomplished throughout the country. It was a most gratifying and interesting experience.

Our aim continues to be Leadership in Community Health. The varied program of the Auxiliary makes it possible for every member to choose the field for her contribution to her community. Be a good member! Be informed!

The Fall Board Meeting and School of Instruction for all state officers, chairmen, county presidents, officers and chairmen and all members of the Auxiliary, will be held at the Curtis Hotel, Minneapolis, Tuesday, October 4. It is the new members, willing to assume leadership, who will be our new county officers and chairmen, and many will continue on to State and National offices. To meet the needs of these new officers, our School of Instruction is planned. Well-informed officers, committee chairmen and members, will produce a progressive organization.

Interesting speakers are planned, including our National Auxiliary President, Mrs. Mason G. Lawson, who will be our luncheon guest speaker. She is most delightful and will be an inspiration for us as we start our new year.

Further details will follow, but save Tuesday, October 4. I will be looking forward to seeing you. I wish you success in all your Auxiliary activities this year—1955-56.

MRS. H. H. FESLER
President

Of General Interest

Hastings State Hospital acquired a new acting superintendent in mid-July. **Dr. Nelson J. Bradley,** superintendent of Willmar State Hospital, is now serving as acting head at Hastings in addition to continuing his duties at Willmar. Since the resignation of **Dr. Ralph Rossen** last fall, the Hastings post has been filled by superintendents and personnel from the other state hospitals.

* * *

Dr. Alf K. Stratte, Pine City, has been given the state's highest award, the Minnesota Medal of Merit. Presentation of the award was made by Governor Orville L. Freeman at Camp Ripley, where Dr. Stratte was senior surgeon during training exercises for the Minnesota National Guard.

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Miss Caryl Hoyer and **Dr. Deno J. Wedes,** St. Paul, were married at Arlington Hills Lutheran Church, St. Paul, on June 18.

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Miss Mary Lou Mulcahey and **Dr. Eugene C. Ott,** Minneapolis, were married at Annunciation Catholic Church, Minneapolis, on July 23.

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Dr. Charles Bolsta, retired Ortonville physician, was recently presented with a printed testimonial by the Medical Alumni Association of the University of Chicago in recognition of the sixtieth anniversary of his graduation from Rush Medical School.

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Dr. E. S. Palmerton, formerly of Fergus Falls, is now practicing at Rapid City, South Dakota. An ophthalmologist, Dr. Palmerton was associated with the Park Region Medical Center at Fergus Falls for the past two years.

* * *

Dr. George L. Berdez, who retired on July 1 as pathologist for Miller Memorial Hospital, Duluth, was honored by the hospital medical staff at a testimonial dinner the preceding evening. Principal speaker at the dinner was **Dr. E. T. Bell,** emeritus professor of pathology at the University of Minnesota.

Dr. Berdez has served as pathologist for more than a dozen hospitals since he arrived at Duluth in 1923. He plans to continue his service at a few hospitals while "slowing down" for another year.

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Dr. and Mrs. Fred A. Figi, Rochester, left by plane for Europe on July 30. During a six-week tour of the continent Dr. Figi presented a paper at the First International Congress of Plastic Surgery in Stockholm, Sweden.

* * *

Dr. Wilford J. Deweese, Bemidji, provided more than a physician's usual services when he saved the life of a seven-year-old girl at Lake Bemidji on July 9. Marshall Deweese, aged eight, saw the girl drowning and called his father, who was working on a boat nearby. Dr. Deweese plunged into the lake, found the child on the bottom in eight feet of water and brought her ashore unconscious. Artificial respiration revived her.

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Dr. and Mrs. W. G. Benjamin, Pipestone, with their two daughters spent July and August on a trip through Europe. During his absence Dr. Benjamin's practice was conducted by **Dr. Edgar Gamm** of St. Paul.

* * *

Governor Orville Freeman has appointed **Dr. Frank H. Krusen,** Rochester, as chairman of a newly formed advisory committee on vocational rehabilitation. The committee will try to help an estimated 80,000 disabled persons in Minnesota become "contributing members of society."

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A biographical sketch of **Dr. Carl Barton Nelson,** Minneapolis, appeared in the Town Toppers column of the *Minneapolis Star* on July 21.

* * *

Dr. Edwin T. Maitland, Jackson, attended a reunion of all past interns of Broadlawn Hospital at Des Moines, Iowa, late in June.

* * *

Dr. Victor Johnson, director of the Mayo Foundation, Rochester, was the principal speaker at commencement exercises for the first summer session at the University of Minnesota on July 14.

* * *

Resignation of **Dr. Howard L. Horns** as assistant dean of the medical sciences and associate professor of medicine at the University of Minnesota on September 1 has been announced by **Dr. H. S. Diehl,** dean of medical sciences.

Dr. Horns, who became assistant dean in 1949, succeeding **Dr. Myron M. Weaver** in the post, is now associated with the Nicollet Clinic in Minneapolis. He recently completed a two-year tour of duty with the Army. He will continue clinical teaching in the medical school on a part-time basis.

* * *

Dr. John M. Streitz is now associated with **Dr. M. M. Fifield** in the practice of urology in Duluth. Dr. Streitz recently completed a residency in urology at the University of Minnesota Hospitals and the Veterans Hospital, Minneapolis.

* * *

An open house celebration was recently held by residents of Cyrus in honor of **Dr. Herman Linde,** who has practiced in the community for fifty years. Numerous gifts and messages of congratulations were presented to Dr. Linde.

Dr. Robert E. Priest, Minneapolis, filled several speaking engagements this summer. At a meeting of the Lyon-Lincoln County Medical Society at Marshall he spoke on "Treatment of Hoarseness." Later he discussed "Treatment of Ear, Nose and Throat Disorders by the General Practitioner" at a meeting of the Tri-County Medical Society at Litchfield and at the Range Medical Association meeting at Grand Rapids.

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Principal speakers at a meeting of the Minnesota Society of Neurology and Psychiatry in St. Paul on September 13 were **Dr. Robert P. Jeub** and **Dr. Jennings C. L. Peteler,** both of Minneapolis.

* * *

Eighteen students trained as **laboratory aides** are being graduated by the General Extension Division of the University of Minnesota this month. Their training consisted of six months of classes at the university and six months of practical training in selected hospital laboratories. In the one-year course they were trained to do most routine medical laboratory tests and are best qualified to work in a physician's office or to assist a medical technologist in a hospital or clinic laboratory.

Information about students or the training program can be obtained from Verna Rausch, Assistant Professor of Medical Technology, C205 Mayo Building, University of Minnesota, Minneapolis.

* * *

At the annual convocation of the American College of Chest Physicians in Atlantic City this summer, the following Minnesota physicians were awarded fellowship certificates: **Dr. James R. Fox,** Minneapolis; **Dr. William F. Mazzitello,** St. Paul; and **Dr. John R. McDonald, Dr. R. Drew Miller,** and **Dr. Gustavus A. Peters,** all of Rochester.

* * *

Dr. Carl O. Thompson, Hendricks, has been appointed coroner by the local board of county commissioners.

* * *

Lt. Col. William F. Sheeley, chief of psychiatric services at the Air Force School of Aviation Medicine, Randolph Field, Texas, has been appointed superintendent of Hastings State Hospital. It was expected that Dr. Sheeley would take over at the hospital by the end of this month, following his discharge from service. The Hastings institution has been without a permanent superintendent since **Dr. Ralph Rossen** resigned last November. Dr. Sheeley was a resident in psychiatry at the University of Minnesota Hospitals from 1950 to 1953.

* * *

Dr. Frank D. Mann, a member of the staff of the Mayo Clinic, Rochester, since 1947, has become associated with the Palo Alto Hospital, Palo Alto, California. Dr. Mann, a son of **Dr. and Mrs. Frank C. Mann** of Rochester, is a clinical pathologist.

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Principal speaker on "The Doctors Round Table," a television program on WCCO-TV on August 28, was **Dr. John P. Medelman,** St. Paul, who discussed the value of routine chest x-rays for all hospital admissions.

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Dr. and Mrs. H. M. Juergens, Belle Plaine, left on August 24 for a tour of Europe. During the trip they plan to attend the World Medical Congress in Vienna, Austria, during the last week of this month.

* * *

Dr. Donald P. Fox, Minneapolis, has been commissioned a medical missionary by the Lutheran Church. With his family he sailed on September 14 for England, where he will study tropical medicine for five months before going on to Tanganyika, East Africa.

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Dr. Andrew C. Erlanson, St. Paul, has been appointed a pediatrics consultant for the Minnesota Department of Health's maternal and child health section. Dr. Erlanson recently completed a three-year fellowship in pediatrics at the Mayo Clinic.

* * *

Dr. Arthur J. Henderson, St. Paul, has been appointed coroner of Ramsey County to fill out the unexpired term of Dr. Carl Ingerson. Dr. Henderson has been a deputy coroner for ten years.

* * *

Dr. K. W. Covey, Mahnomen, has announced that he will discontinue his practice about January 1 to accept a residency in orthopedics at the Mayo Clinic. Dr. Covey has practiced at Mahnomen since 1944.

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Principal speaker at a meeting of the Rotary Club in Duluth recently was **Dr. Gordon J. Strewler,** Duluth, who discussed "Sidelights on Maturity."

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Dr. and Mrs. H. C. Habein, Rochester, returned in mid-August from a six-week vacation in Europe. During the trip they visited their son, Dr. Peter Habein, who is stationed at an Air Force hospital in Germany.

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Dr. Thomas H. Johnson, a graduate of the University of Minnesota Medical School, took over his duties in mid-August as resident physician at the state prison at Stillwater.

* * *

Dr. Corrin H. Hodgson, Rochester, left on August 22 on a special mission to Africa as medical advisor for an expedition headed by Congresswoman Frances P. Bolton. Object of the group, which will return in November, is to study economic, social and health factors for the House Committee on Foreign Affairs.

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The Minnesota Safety Council has awarded a certificate of recognition of long service to **Dr. F. J. Hirschboeck,** Duluth, medical representative on the council. The award was made at the annual meeting of the council in Duluth on August 19.

* * *

Dr. William M. Feigal has been elected president

(Continued on Page 662)

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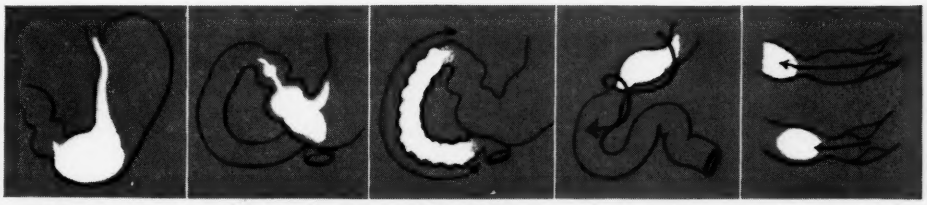

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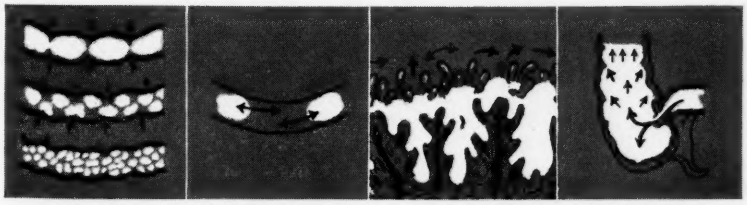

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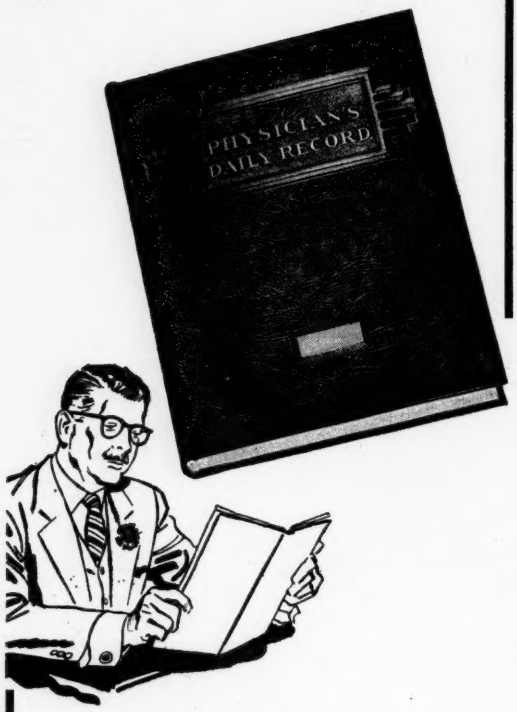

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(Continued from Page 660)

of the medical staff of Northwestern Hospital, Thief River Falls. Named as vice president was **Dr. Daniel Greene,** with **Dr. George Martin** as secretary.

* * *

Mrs. Dorothy B. Leven, wife of **Dr. N. Logan Leven,** St. Paul, died on August 6. For many years Mrs. Leven was active in social and welfare work in the Twin Cities. She was married to Dr. Leven in 1930.

* * *

Dr. and Mrs. F. H. Ellis, Jr., Rochester, left on August 22 for a five-week tour of Europe that was to include two weeks in Russia. Dr. Ellis plans to meet with Russian surgeons in Moscow and Leningrad and exchange information on surgery with them.

* * *

A check for $53,000 for heart research was given to the University of Minnesota by the Minnesota Heart Association on August 16. Accepting the check, which was the first installment of $105,644 allocated for heart research projects, was **Dr. Harold S. Diehl,** dean of medical sciences.

NEW LOCATIONS

Dr. Arnold M. Berg, formerly of Hawley, has become associated in practice with **Dr. D. O. Berge** at Roseau.

Dr. Robert Carlson, who recently completed his internship in Portland, Oregon, has joined the staff of the Davis Clinic in Wadena.

Dr. Robert C. Ahlstrom, who interned at Ancker Hospital, St. Paul, has become associated with **Dr. W. T. Nygren** in the Braham Clinic, Braham.

Dr. G. H. Purves, formerly of Hendricks, has become associated in practice with **Dr. Waldo P. Anderson** in Buffalo.

Dr. Clayton R. Green has taken over the office of **Dr. John P. Cooper** in Excelsior. Dr. Cooper is doing postgraduate work at the University of Minnesota.

Dr. Paul T. Grimes, formerly of Harrisburg, Pennsylvania, has become associated in practice with **Dr. Norman Haugan** in Park Rapids.

Dr. Ernest J. Aulick, formerly of California, has opened offices for the practice of medicine in Belgrade.

Dr. Harry F. Burich, formerly of La Crosse, Wisconsin, has joined the Olmsted Medical Group in Rochester as a general surgeon.

Dr. Charles J. Hedlund, formerly of Los Angeles, California, has become associated in practice with **Dr. F. C. Closuit** in Aitkin.

Dr. Fred Colosey, formerly on the staff of the Shipman Hospital in Ely, has moved to South Bend, Indiana, where he is now practicing.

Dr. Lloyd T. Wood, who recently completed his internship in Detroit, Michigan, has become associated in practice with **Dr. N. M. Mensheha** at Forest Lake.

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*Farley, W. J.: Oxytetracycline in Pediatrics, Internat. Rec. Med. *168*:140 (March) 1955.

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(Continued from Page 662)

Dr. Theodore M. Gill, who recently completed a residency in ophthalmology at Minneapolis General Hospital, has become associated in practice with his father-in-law, **Dr. F. G. Folken,** in Albert Lea.

Dr. H. W. Henry, after two years in the Air Force, has returned to Hinckley and reopened his offices for the practice of medicine.

MINNESOTA BLUE SHIELD-BLUE CROSS

According to statistics just released from Minnesota Hospital Service Association (Blue Cross) for the month of June, 1955, there were 14,684 hospital cases paid in the amount of $1,678,891 for a total of 91,096.5 days of patient care.

During the first six months of 1955, Blue Cross subscribers have been provided with 521,079.3 days of hospital care. Total benefits paid for this six-month period amounted to $9,524,072.

The figures also revealed a decrease in upper respiratory cases during the first six months of 1955 over the same period in 1954. For example, during the first six months of 1954, Blue Cross benefits were paid for 6,911 tonsillectomies, while there were only 4,507 such cases during the same period in 1955.

Since 1933, 11,000,085.9 days of hospital care have been provided for Blue Cross members, representing over $120,000,000 in benefits.

Within the next two months Blue Cross and Blue Shield "Scotchlite" highway signs will be erected in two-hundred strategic locations throughout Minnesota.

These signs will prominently display the Blue Cross and Blue Shield emblems in blue scotchlite with the words Blue Cross and Blue Shield in silver scotchlite on a blue background. The slogan "You Need Both" is in red letters on a yellow background. These signs will appear as handsome daylight displays, and at night will glow brightly when caught in the beam of passing automombile headlights. They will be constant reminders to all Minnesotans of the importance of Blue Cross and Blue Shield in their daily lives. Located over the whole state, they broadcast the need of effective protection for hospital and doctor bills.

Integrated with this program of highway advertising, 23 daily, and 80 weekly newspapers throughout Minnesota, in addition to Twin City papers, will carry the Blue Cross-Blue Shield story. More widespread use of daily and weekly newspaper advertising by Minnesota Blue Cross and Blue Shield coincides with an expanded national advertising program of the Blue Cross and Blue Shield Commissions. This program is extended to include national general magazines, as well as business and press magazines. Also, radio and television stations throughout the state, in addition to those of Minneapolis, Saint Paul, and Duluth, are carrying spot advertising and announcements concerning the effectiveness of Blue Cross and Blue Shield in meeting hospital and doctor bills.

Insofar as Blue Shield, the doctor's plan, is concerned, the scotchlite highway signs are part of a program to keep before the public the sponsorship of a prepayment medical care plan by the members of the medical profession of the State of Minnesota.